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THE OBJECTIVES OF THE FDA'S OFFICE OF GENERIC DRUGS

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ABSTRACT

I use variation in approval time for generic drugs to shed light on the objectives of the federal agency in charge of granting entry permission for these drugs (FDA). Applications belonging to firms later found to have engaged in fraud or corruption were approved nine months faster on average, controlling for other characteristics, indicating that illegal behavior was effective in reducing approval times. The FDA approved applications for large revenue markets faster; this is the only evidence that the agency is taking consumer surplus into account, but it is also consistent with a response to producer surplus and application quality. Order of entry into a drug market is insignificant in predicting approval times due to the offsetting effects of social surplus and FDA learning. The FDA appears to avoid complaints from constituent firms by preserving the entry order of applications. FDA resources clearly affect approval times; this appears in the year effects after the generic scandal (much slower) and in the agency's use of slack provided by applications submitted before patent expiration. After the scandal the FDA appears to care more about the risk inherent in a product and discounts a firm's pre-scandal technical experience. Overall, the results provide most support for an agency responding to bureaucratic preferences, complaints from constituent firms, and risk to consumers, rather than trying to maximize classic measures of social surplus (absent risk considerations).

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I. Introduction

In unregulated markets, a competitor interested in entering the market after patent expiration simply does so. In regulated markets, such as the pharmaceutical industry in the United States, a manufacturer must receive approval from the Food and Drug Administration (FDA) before it may legally make and sell its product. Therefore, the process by which the FDA regulates entry and its implementation of laws promoting competition affect consumer welfare and are of policy interest. Additionally, the way firms interact with the agency and the strategies they adopt to gain approval shed some light on firm behavior in the face of regulation.

In this paper I seek to examine the behavior of the FDA, in particular, the time it takes the FDA to approve generic drug applications, and infer from that behavior the goals of the regulatory agency. The two most important groups the agency should be seeking to please are consumers and producers. Both groups prefer applications to be approved quickly, although consumers also care that unsafe drugs are not approved. Speed was especially important during this time period my data cover because generic firms were generally not applying early relative to patent expiration. Instead, many generic firms submitted applications after the relevant patent had already expired. Thus, the quicker FDA approval arrived, the sooner the market became more competitive. Speed is more valuable in larger markets where there is more social surplus. Producers prefer speed for their own product and not for anyone else's and may use their political clout to influence the agency in their favor. Additionally, reviewers at the agency may have personal objectives which do not match those of the agency but affect approval times. I discuss the motivations of the FDA and its employees in more detail and review the existing evidence of what the agency's objective function might be. Then I look at characteristics of generic drug approvals from 1984 to 1994 to see whether there is empirical support for any of the alleged motivations of the FDA.

A feature of the time period in which my data are generated is a strong regulatory tightening that occurred in 1989. For several years starting in 1989 sloppy and/or illegal activities were uncovered in the generic drug approval process. Firms were not adhering to established manufacturing standards or were explicitly deceiving the FDA about their product. The industry upheaval caused by the "generic scandal" significantly altered the approval process at the Office of Generic Drugs of the FDA. The (arguably exogenous) change in regulatory stringency makes a good natural experiment in which to test for changes in regulatory goals.

The results confirm that illegal behavior on the part of applicants was successful in lowering approval times by an average of approximately nine months. Applications for large revenue markets are

approved more quickly, although the order of entry into the market, something that affects both producer and consumer surplus, insignificantly affects approval time. The FDA appears to be taking steps to minimize complaints from constituent firms by approving firms in the order in which they applied. After the scandal, approval times lengthened dramatically and the FDA becomes more cautious. Potentially dangerous drugs are approved more slowly, past experience with a drug no longer lowers approval times, and large established firms have quicker approvals.

An unfortunate feature of the data is that I observe only approved applications, not those that were submitted to the FDA, but not yet approved for whatever reason. This affects the interpretation of the results and limits the econometric applications. The remainder of the paper is laid out as follows. The available evidence on the FDA is described in Section 2, the Office of Generic Drug's objectives and the specification to be estimated are discussed in Section 3. Section 4 explains the regulatory environment. The data are described in Section 5, while initial results are presented in section 6. Section 7 develops and estimates a more detailed econometric model; Section 8 concludes.

2. Literature Review and Available Evidence on Agency Objectives

The actions of the FDA are at the center of the analysis, so it is necessary to form some idea of what the objective function of the agency might be. Baron and Besanko (1984) suggest that regulators maximize a weighted sum of producer and consumer surplus, where consumer surplus gets a higher weight due to consumers' strength in the political process. However, the characteristics of much regulation biases it in the direction of serving industry interests because any particular regulatory decision is likely to have a very strong impact on any firm in the industry but a small impact on any particular consumer. The firm therefore has more incentive than a consumer to organize and attempt to lobby the agency. In the extreme case when the regulator always acts to benefit its regulated firms, the agency is said to be "captured" by industry (Stigler (1971)). The available evidence (discussed below) provides some support for the effects of both producer and consumer surplus on agency decisions.

Weingast and Moran's (1983) model of congressional committees proposes that agency bureaucrats act according to the preferences of their congressional committee members in order to protect the agency's budget and power. Niskanen (1971) says that an agency must avoid doing harm to an industry in order to protect its budget and grow; agency actions are directed at maximizing the budget. These latter two theories have less support in the existing literature, so I will not focus on them in this paper.

Several empirical papers examine the objectives of the FDA but principally focus on new drug approvals. Olson (1993) uses the approval behavior of the FDA to separate out which constituent

(congress, consumers, firms) signals it responds to. She estimates a three-equation model where the dependent variables are generic drug, branded drug, and device approvals. She finds that the number of generic approvals depends on the (entire FDA) budget and the number of generic applications received, with a larger budget or more applications producing more approvals. Additionally, she finds that the generic scandal significantly reduced the number of generic drug approvals. Olson concludes that when the agency expects higher stock market rate of return for generic firms, it tends to grant more approvals since it responds to signals from these firms. However, in this case the causality may go the other way since an approval typically increases a firm's stock price (see Bosch (1994)). She finds none or very weak evidence that employment in the industry, the death rate in the population, or congressional preferences affect generic approvals. Her evidence suggests that strong predictors of approvals are resource factors such as the scandal and the budget, while general consumer concerns and political oversight are weaker forces.

Dranove (1994) examines the speed of approval of branded products and asks if "important" products get approved faster than unimportant products. He finds that important products do get approved in a shorter time from international patent filing, but that this has been true since the 1950's (before the stricter rules on approvals and before the FDA's important drug classification), and is also true internationally. In particular, a drug's importance in a market sense (revenue) rather than a scientific sense is what seems to matter. Dranove concludes that rather than the FDA being very sensitive to consumer and producer surplus, innovators increase investment in the quality of the application when the rewards are bigger. He also finds that the experience of the firm in guiding applications through the FDA has no impact on approval times, but local (national) manufacture of the drug tends to speed the approval process, suggesting agencies respond to local producer surplus more than foreign producer surplus.

Olson (1997) looks specifically at whether applicant characteristics explain new drug approval times from 1990-1992. The short time period means there is little structural change during the sample, but limits the sample size (72 new chemical entities approved). She finds that applicants who do more R&D (R&D/sales) and are focused in the pharmaceutical industry (pharmaceutical sales/total sales) experience quicker approval times. She interprets this as evidence for responsiveness of FDA reviewers to a firm's expertise and reputation for good science. Additionally, the data indicate that firms with more applications currently pending at the FDA, and therefore perhaps better communication channels with reviewers, have faster approvals. Larger firms and foreign firms also experience faster approvals; larger firms may have more political influence, but interpreting the foreign firm result is difficult. Year and therapeutic class effects are strongly significant in explaining approval times also.

Using an in-depth interview method to gather data, Quirk (1980) presents evidence of the concerns and perceptions of officials at the FDA. Quirk, while primarily focusing on the branded (new molecule) side of the agency, claims that lobbying to members of Congress or the President to affect the agency's powers or budget is uncommon. This is consistent with Olson's evidence that the agency budget has no effect on branded drug approvals. In contrast, FDA officials claim that threats to the budget come from public displeasure. Quirk also finds FDA officials are not concerned about influence on the appointment process that might affect the preferences of those in power.

Another alleged problem with agencies is that officials act favorably toward industry in order to obtain a job in industry later in their careers.[1] Quirk provides evidence that professional abilities gain a person a good reputation in the pharmaceutical industry and only really radical viewpoints can hurt a career. On the other hand, regulators at the FDA have regular meetings with industry representatives, develop a long term relationship with them, may come to like them personally and share opinions with them, and also rely on them for a good deal of information. Groups opposed to corporate goals have no such regular intercourse with the agency and therefore may not exert as much influence on regulators' decisions.

Consumer activism on the issues of speed and safety has great influence on regulators at the FDA according to Quirk. However, the instances he discusses in which angry consumers organize against the agency are those where a potentially life-saving drug is not being given initial approval. Generic drug reviewers do not face this pressure. Consumers are less likely to organize and protest that a drug is expensive because of slow generic approvals. However, the problem of an incorrectly manufactured drug causing large-scale harm to the public remains in the case of generic drugs. Reviewers concerned with consumer safety therefore examine drugs carefully, which takes time. Additionally, if reviewers are concerned about their own employment, they will be very averse to approving drugs that could be dangerous, since this might cause them to be fired. Being speedy and accurate in approvals, however, does not yield a symmetric risk of a great employment outcome. Therefore, there exist personal incentives for caution and delay that are likely to be in excess of what consumers prefer. A mitigating factor is that the substance has been used as a therapy for years already, so the reviewer need only be concerned with whether the new applicant possesses the manufacturing skills and facilities to replicate the branded drug accurately, not whether entirely new chemical entities are safe and effective.

Delay

[1] This is known as the 'revolving door' theory.

The nature of the FDA's task may also contribute to delay that harms both producers and consumers. Drug applications are complex and evaluating them with a team of specialized reviewers is difficult, time-consuming, and still results in lots of uncertainties. The FDA must review the testing done by the applicant to look for dishonesty or ordinary mistakes caused by the complexity of the problem. Additionally, pharmaceutical firms are likely to offer the more competent bureaucrats employment with higher salary and/or status. The turnover of good employees plus the additional training costs imposed on the agency contribute to delays in drug approvals. Since the probability of a mistake goes down with more time and effort on the part of the reviewer, a regulator will be biased in favor of delay. The tendency to delay is reinforced by Congress which periodically investigates the FDA and concludes the agency is not tough enough on industry, according to Quirk.[2]

In summary, there is some evidence that FDA cares about producer surplus and consumer safety. However, bureaucrats' risk aversion causes delay in approvals. Avoiding mistakes furthers the regulators' goals of maintaining both their own reputations and the reputation of the agency. Time is the outcome variable that reflects which of these goals is more important for any given approval. Analysis approval times in conjunction with application characteristics should reveal the agency's preferences. Since the agency would essentially always prefer to delay, those drugs that are approved faster than others will have characteristics attractive to the agency such as increasing consumer or producer surplus, reducing political pressure, or increasing reviewer utility.

3. Model of the Objectives of the Office of Generic Drugs

. The external signals model is proposed by Joskow (1974) and discussed in some detail in Noll (1985) can be modified to fit the situation of the FDA's Office of Generic Drugs. Joskow and Noll model an agency as maximizing a weighted sum of all signals, or feedback, from its constituents. Feedback in the case of the FDA's Office of Generic Drugs might come from regulated firms, congress, consumers, physicians, managed care organizations, etc. In particular, the external signals model allows for the influence of what Olson (1995) refers to as "hassles." Complaints from constituent firms about agency behavior can be costly to the agency by triggering interference from political actors or activist groups. These hassles are negative feedback that the agency attempts to minimize when it chooses its behavior. An important additional force that affects agency decision-making is the utility of the bureaucrats themselves. The agency will respond to outside preferences as well as the personal preferences of those

[2] Other similar reasons Quirk gives for being cautious in approvals are protecting the President from adverse publicity and maintaining the morale of the agency.

inside the agency. Below is an empirical specification of the external signals model that is appropriate for my data, approval times of generic drug applications.

Each application can be sped up at a marginal cost to the agency, and that additional speed will generate a feedback gain from agency constituents, or marginal benefit. In particular, an agency with limited resources deciding where to spend the marginal resource will direct it to the application with the highest net marginal feedback. In order to rule out extreme solutions – the application is approved in one day – I will assume that moving away from a standard approval length eventually causes cost to increase faster than benefit. Thus, the agency would experience extremely high political and scientific costs if it approved an application in one day, costs that overwhelm any beneficial signal coming from the applicant firm. At the optimum, the agency has adjusted approval times such that marginal benefit equals marginal cost for all applications.

The dependent variable of interest is the time taken to approve the application. The year the application is submitted, therapeutic dummies, and drug dummies are the basic elements (Z) of an estimation of the mean expected time to approval since this covers technical characteristics and resources available that year at the FDA. Deviations from standard approval times are in the control of the agency and should be affected by the feedback the agency expects to receive from its constituents. In equation (1) below, X is the matrix of characteristics that measure either marginal benefit or marginal cost to speeding up the application while technical features of the drug serve as controls. The characteristics in the X matrix fall into the groups discussed above, producer surplus, consumer surplus, and reviewer preferences. The linear form ($X\beta$) allows the estimated coefficients to convert each variable to the appropriate units, while summing over variables produces the item of interest, the net benefit to speed for that observation.

$$X\beta = X_{ps}\beta_1 + X_{cs}\beta_2 + X_{rp}\beta_3 + Z_{tech}\delta_4 + Z_{resources}\delta_5$$

The variables that measure these characteristics are discussed in detail in Section 7 of the paper. I will model influences on approval times with the following hazard model: [3]

$$h(t) = h_0(t)\exp(X\beta + Z\delta)$$

where h(t) is the instantaneous probability of 'failure,' or in this case, approval by the FDA.

[3] This expression is a Cox proportional hazard model.

Another aspect to this analysis is that the applicant has some impact on the application time, although it is ultimately controlled by the FDA. For example, the quality of the ANDA is likely to be an important factor in how quickly the application is approved; quality lowers the marginal cost (approving a dangerous drug) to speed. However, application quality cannot be observed. Quality is likely to be correlated with observed characteristics such as market size. Since there is no proxy for unobserved quality, interpretation of the effect of market size on approval times will include FDA concern for consumer surplus as well as the effect of producer surplus on application quality.

Secondly, part of reviewer preferences is the amount of risk posed by a mistake on the part of the reviewer. A measure of the potential risk of an application is very difficult to construct and should ideally include a medical evaluation; creating such a measure is beyond the scope of the current paper. However, the generic scandal provides a discrete moment when perceptions of risk changed greatly. After that point, reviewers' priors on the existence of mistakes in an application and therefore the potential for a badly manufactured drug increased sharply. I assume that reviewers at the FDA became much more sensitive to the likelihood of approving a fraudulent application at this time, and that their sensitivity lasted for several years. In the context of the model, the marginal cost of speed likely rose due to the scandal. The changes probably depended on the FDA's new assessment of the risk associated with any given characteristic. Therefore, the explanatory variables may have different effects on approval times before and after the scandal. I estimate the model on two separate samples, applications submitted before 1990 and applications submitted in 1990 and later.

4. How a Generic Drug Application is Approved

The approval process for generic drugs changed markedly in 1984 with the passage of the Waxman-Hatch ("Drug Price Competition and Patent Term Restoration") Act. The Act balanced the interests of branded manufacturers and generic manufacturers. The gain to branded drugs was the provision of patent extensions when the FDA took an exceptionally long time to approve a new drug. Long approval times could leave very few patent-protected years in which to sell the drug on the market. To balance the increased profits this change would bring to innovator firms, the cost of generic entry was significantly reduced for a large group of drugs. Instead of redoing the clinical trials proving the substance to be both safe and effective, which are required of the innovator, a generic product could be approved by showing its product was bioequivalent to the branded product. Bioequivalence tests are *much* cheaper than original safety and efficacy tests.

The more limited tests that generics have to complete to enter the market comprise an Abbreviated New Drug Application (ANDA). Getting an ANDA approved involves convincing the FDA that the

manufacturing process is correct and the final product is virtually identical to the brand.[4] Some specific activities involved in filing an ANDA include certifying the suppliers of the bulk chemical, producing test batches, arranging independent laboratory testing of the batches, and allowing the FDA to inspect equipment and procedures. The Waxman-Hatch Act was passed in the fall of 1984 and took effect at the FDA on November 24, 1984. Generic firms keeping track of legislative developments could have started to prepare ANDAs in the summer of 1984 in anticipation of a regulatory change. The data I use for this project begin in 1984 partly because the Act required the FDA to keep track of more patent data as of that time and partly because the regulatory change suddenly opened up a huge market for generic firms. Generic firms responded strongly to the new legislation by submitting ANDAs in record numbers. The number of ANDA submissions (that were eventually approved) by quarter is reported in Table I.

In mid-1988 a complaint was made by Mylan, who thought its competitors' applications were moving through the FDA faster than its own. Mylan and others questioned the integrity of FDA reviewers. Preliminary investigations into FDA practices were met with hostility by the agency, prompting more investigations. In 1989 it was discovered that employees of several generic firms had been bribing FDA reviewers to speed approval of their applications. Law enforcement pursued firms in the industry for other illegal activity. Some firms had had submitted the re-coated branded product as their own to independent labs for testing, (the branded product naturally did very well in tests comparing it to the brand!), other firms had falsified or destroyed documents to cover up these activities or to expedite approval of an ANDA. The original and follow-on investigations over the next two years caused employees of at least nine firms to plead guilty or be found guilty of various illegal actions.

These revelations shook public confidence in the generic drug industry and the FDA. Many reviewers at the agency were fired, the Office of Generic Drugs was restructured, and the remaining reviewers were cautious in approving products for several years. The firms that had obtained ANDAs illegally had their products withdrawn from the market until they could show that each product met FDA standards. The FDA stepped up enforcement of Good Manufacturing Practices and increased the number of inspections. The average number of inspections per firm increased from 2.5 in 1987 to 3.9 in 1990, while the average number of days per inspection also rose from 11 to 19.[5] Table I clearly shows the effect of the scandal on approvals in 1990; the agency took several years to fully recover from the slowdown. In

[4] A generic product is tested to make sure it has the same dissolution properties as the brand (dissolves in a beaker at the same rate) and is tested on healthy human subjects to make sure the active ingredient reaches the same organs in the same amount and same time as the brand.
[5] Zarembo, p385.

the empirical work below, I look for the scandal's influence on approval times before and after its discovery.

5. Data

I have data on all ANDAs approved between 1984 and 1994, inclusive. Each observation includes the name of the applicant, the drug, its form, route, and concentration, the date of ANDA submission to the FDA, date of tentative approval, date of permanent approval, and whether the firm withdrew from the market at a later date. Submission and approval dates are tabulated in Table I; applications that are submitted and approved in the same calendar year are on the diagonal, while applications with longer approval times appear further off the diagonal.

A major feature of the data is that the FDA will not release any information on applications that have *not yet been approved*. Thus if a firm applied and then dropped out, applied and was denied, or applied and is still waiting to be approved, I have no information about the application. This is obviously less than ideal since it creates an important selection effect. However, since the data on applications that were not approved will never be made public, the best course of action is to learn as much as possible from the available data, keeping it mind its limitations. For example, those firms that drop out are the ones most likely to have long approval times (due to problematic or low quality applications); the omission of problem observations means that the observed mean approval times need to be interpreted carefully. Approved ANDAs submitted in 1992-1994 are in the sample because they were approved by the end of 1994. Thus the dataset has no "slow" applications in these years. Similarly, only applications submitted in November 1984 or later are included, so there are no 1984 approvals and 1985 approvals are also quick. These patterns are reported in Table III.

The dataset is complete; it contains all ANDAs that have been approved since 1984. The dataset lists the ingredient or ingredients in the medicine; I code each combination of ingredients as a separate drug. The form of the drug is one of about twenty terms: capsule, injection, solution, swab, paste, and extended release tablet are examples of the different kinds of form available. I condense these categories into five basic forms noted in Table II. A separate ANDA must be submitted for each concentration of the drug the firm wants to make and sell. However, I see no cases of a firm applying for the 25mg tablet and not the 50mg tablet if the two strengths have the same patent expiration date. Therefore, the empirical work focuses on the drug-expiration date level and ignores multiple concentrations because they do not provide significant additional information.

The speed at which the FDA approves an application can be measured by the time between the submission date and the final approval date or, if it exists, the tentative approval date. Tentative approval is granted when the firm has satisfied all FDA requirements but the relevant patent or exclusivity protection on the branded product has not expired yet. Final approval is granted later when the patent expires, and at that time the firm is free to sell the product. If the firm is not "early," it passes the FDA requirements after legal protection of the brand has expired; therefore, no tentative approval date exists. Approval times by form are listed in Table II.

I also know when the applicant submitted its application relative to patent expiration. The FDA provides some information on patent expirations and also on its own exclusivity periods. As mentioned above, these periods of protection from generic entry are granted for delay in processing an NDA and also for new routes or strengths of a drug. I augment the FDA information on patent and exclusivity expirations with information from telephone conversations with patent lawyers. The timing of an application relative to patent expiration reveals whether a firm has applied early or late.

Some drug markets in the sample had experienced generic entry by the time the regulations changed. (The Waxman-Hatch Act lowered the cost of entry dramatically, but some entry occurred under the previous rules.) I obtained revenue data for all drugs in the sample from IMS America, a data collection firm. The figure I use is the sales of the brand in the year before patent expiration or 1984, whichever comes later. For those drugs with entry before 1984, I use the total market sales in 1984, both brand and generic.

The entire original dataset has close to 5000 observations. For several reasons, I eliminate certain categories of ANDA to end up with a total of 1399 observations. Applications received before November 1984, but granted between 1984 and 1994 are removed from the dataset. Some ANDAs allow firms to make "bulk" products; bulk products are an intermediate step *en route* to the final pharmaceutical product. The markets are not the same, so those ANDAs are not included in this study. A separate ANDA is required not only for each concentration, but for each packaging type in the case of injectables, and sometimes for different manufacturing plants. These rules reflect technical concerns of the FDA and do not define distinct submarkets in an economic sense. Therefore, I compare observations to locate and remove the duplicate ANDAs in my dataset, keeping the application with the earliest submission date. As mentioned above, I keep the concentration submitted first and drop any applications for additional concentrations submitted by the same firm for the same drug with the same patent expiration date. This process removes a great number of observations since the average drug comes in about 2.5 different concentrations. ANDAs where the applicant is also the original innovator are deleted (mostly antibiotic drugs). A more difficult problem is that in 1984 distributors could still receive "repacking" ANDAs,

ANDAs that neither required nor permitted manufacturing. This type of ANDA was no longer granted by early 1985, but earlier instances must be removed from the dataset. I have eliminated cases where the firm was known to repack only and also those observations submitted in November or December 1984 where the ANDA was approved in less than four months time. Finally, there are a few cases where the patent expiration information was inconsistent and abnormal, and these observations could not be used in the estimation.[6]

6. Variation in Approval Times

The first step in the analysis is examining the variance in the time it takes generic firms to gain FDA approval for their products. I run a basic ANOVA intended to reveal sources of variation in approval times. I expect that some drugs are more difficult to manufacture and require more complex tests than others. Therefore approval time should vary with the specific drug. In the same way, the form of the medication and its therapeutic area affect the standards for showing bioequivalence because the different forms are absorbed by the different parts of the body in different ways. The calendar year of submission is crucial in predicting time to approval because of the backlog of cases immediately after the new legislation took effect and also because of the generic scandal. Therefore, drug, form, therapeutic area, and year are included as potential sources of explanation for variance in approval times.

The results of the ANOVAs are reported in Table IV. There is a large amount of variance in approval times and about half of it can be explained with drug, year, and form fixed effects. The most important explanatory variable is year, due to the scandal that occurred about halfway through the sample. The adjusted R^2's are between 0.3 and 0.4, which leaves a significant amount of unexplained variation. Although one might imagine *ex ante* that the drug fixed effects are important, they explain surprisingly little of the variance in time to approval. Therapy and form have the least explanatory power when drug fixed effects are included.

Some generic firms might have a capability in constructing an ANDA, perhaps their research teams are more skilled at the tasks involved. The second ANOVA adds firms to the decomposition to see if they are collectively contributing to explained variation. Firms are jointly significant in explaining

[6] For example, Dipyridamole was made by several generic firms and the innovator before it was discovered that the drug was dangerous, not helpful. The originator found another use for the drug, and patented the new indications. The generics could not legally sell the drug for the new indications and the FDA tried to remove the generics from the market. The generic firms managed to delay the withdrawal through legal maneuvering until the patent date on the indications. At that point, the FDA recorded an official (and by then legal) approval date. However, this date bears no relation to actual actions in the market. A few ANDAs have approval dates that precede the submission

approval times. However, many of the firms in the industry are not independent, but belong to a parent firm which may own other generic or innovator pharmaceutical firms. If a firm has a competency or ability to submit quickly-approved applications, it may lie with the subsidiary, or the organization as a whole may have the skill and submit different applications in the name of different subsidiaries. I repeat the ANOVA with parent corporations rather than applicants as the firm variable in case the subsidiaries or divisions of a corporation act more like one firm. Parent firms do a little bit better in explaining differences in approval times.

I repeat the analysis in regression form as follows in order to examine the specific effects of different years and firms:

$$approval\ time = \gamma_0 + \gamma_1 year + \gamma_2 form + \gamma_3 drug + \gamma_4 therapy + \gamma_5 firm$$

The OLS standard errors have been corrected (White 1980) for heteroskedasticity. The first regression in Table V omits the firm variables and reports both year and form coefficients. As expected, the year coefficients display a strong pattern. The years 1988-90 are slowest, with approval times dropping as applications are submitted later in the 1990's. The strong negative coefficient on 1993 submissions reflects the fact that the sample only contains applications approved by the end of 1994. Overall, the year coefficients correspond well to the mean approval times reported in Table III. The form coefficients display a reasonable pattern also. Pills, the omitted category, are quickest to gain approval. Ocular (eye) drugs are slowest, on average eleven months slower than pills, while injectable, topical, and oral liquids are in between.

The regression in column two adds the firm variables. The year effects are quite stable across the two specifications, while the coefficients on injectable and oral liquid forms change considerably. The change in the form coefficients reflects the empirical fact that many firms specialize in one or more forms, so that controlling for firm absorbs some of the form effects. The dummy variables for drug markets are included in both regressions, but the drug and firm coefficients are too numerous to be reported. However, the firms with the highest and lowest firm dummy coefficients and more than one observation in the regression are listed at the side of Table V. The only therapy coefficients in regression (2) that are not collinear with form and drug are reported there also (analgesics, or painkillers, is the omitted therapeutic category). The results indicate that drugs for hypertension are approved quickly relative to painkillers, while anti-infectives take longer to be approved. If drug variables are omitted, then

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date of the application to the FDA. FDA officials explain that these cases are re-submitted ANDAs for products where standards have changed. The observations are not used in the analysis.

all the therapeutic classes can be used to explain approval times. Although the results of this regression are not reported, four therapeutic categories had dummy variables significantly different from zero: anti-ulcer drugs, hormones, diagnostic agents, and anti-arthritic drugs. The results indicate that a firm can expect the FDA to take about seventeen months longer to approve a diagnostic drug than a pain reliever.

Column (3) reports the base case regression with an additional variable that identifies the effects of illegal activities on the part of some firms. Several of the most active firms in the sample are also firms that were indicted in the generic drug scandal. These indicted firms should have lower firm coefficients than other firms, presumably because their products were approved faster due to bribes. I assume that all firms that acted illegally were caught. A dummy variable, *bad*, equals one for the firms with employees indicted in the affair. The coefficient on *bad* is negative and significant, however, its size -- 425 -- days is somewhat worrying since the mean approval time during the mid-80's was in the low 500s.

The problem is that *bad* firms have no approvals in the early nineties; the FDA likely forced them to withdraw pending applications since even their portfolios of existing drugs were under suspicion. Thus, bad firms do not have the long approval times of other firms in the early 90's and this makes them look "faster" when the whole sample is used. To form a better estimate of the advantage of illegal activity, I rerun a simple specification (drug and firm dummies only) on a restricted sample of ANDAs submitted in 1984-6 and approved before 1990. These results are reported in column four of Table VI. The coefficient drops to a negative 272 days; about nine month's advantage seems to have been gained from bribery or other illegal activities.

7. Characteristics of the Firm, Drug, and FDA, and Estimation of Approval Times

A. Explanatory Variables

With the data I have assembled, I can examine which characteristics of the firm, the drug, and the regulatory agency affect the speed of an ANDA approval. As discussed in the theory section, we expect producer surplus, consumer surplus, reviewer preferences, technical concerns, and resources to be the main determinants of the length of time an approval takes. The following section will describe and define the variables used to measure each determinant.

Lower pharmaceutical prices due to generic competition increase consumer surplus. More competition in large revenue drug markets benefits consumers more than the same change in a smaller market, all else equal. In addition, a generic entrant into a market captures more producer surplus the larger the market (holding the number of incumbents constant). The size of the market is represented by *LnRevenue*, the log of total revenue in a market in the year before patent expiration or 1984, whichever

comes later. Producer surplus should affect approval times in two ways. On the one hand producer surplus may be on the FDA's objectives. Secondly, application quality is a more worthwhile investment for a firm as the size of the market increases. A firm that puts resources into constructing a quality application to start with will have fewer clarifications and revisions to perform for the FDA and its ANDA will be approved more quickly (as in Dranove (1994)). Therefore, we expect application times to drop strongly with the size of the market as consumer surplus, producer surplus and quality of application are all working in the same direction.

The first generic in a market provides the first option to purchase the molecule at significantly lower prices and increases consumer surplus much more than the tenth generic in a market. Therefore, the FDA may benefit society more by being faster with earlier entrants. *OrderOfEntry* is a variable which simply indexes a firm's application date in a drug market; the first applicant gets a one, the second, two, etc.. Prices in generic drug markets decline with the number of generic producers in a Cournot-like fashion, so that earlier entrants likely earn higher margins and more profits – more producer surplus.[7] The existence of more generic entrants in a market reduces producer surplus which also reduces the incentive for firms to submit high quality, and therefore 'fast' applications. We therefore might expect order of entry to have a positive effect on approval time. A weak pattern of this type can be seen in Table VII where mean approval times by entry order statistic are listed.

However, as discussed above, the FDA puts considerable weight on harm done to consumers due to approval of a dangerously manufactured drug. The FDA is not normally in the public eye until a dangerous drug surfaces, at which point it attracts unpleasant and costly public scrutiny. If the agency is cautious and more thorough in reviews of unfamiliar substances, then being the first applicant in a market may result in a slow review.[8] The tenth applicant under this hypothesis will find established standards for testing and manufacturing and experienced reviewers at the agency and, in consequence, a faster review process. In short, those applicants which could potentially provide higher benefits also have higher risks. It is not obvious which effect will be stronger.

It is important to note that producer incentives are more complex than a simple measure of the producer surplus gained by the n^{th} entrant because producer profits are interrelated.[9] For example, the producer of the branded drug would prefer that no application for a generic form of its drug was

[7] The pattern of generic price declines in the number of producers is well established. See Frank and Salkever (1995), Wiggens and Maness (1995), and Caves, Whinston, and Hurwitz (1991) for evidence.

[8] For example, according to FDA officials, there is currently an additional meeting for reviewers and higher-level officials when the first drug in a market is ready to be approved. Although this procedure was implemented after the scandal, there may have been an equivalent informal procedure before the scandal.

approved at all. Since research-based firms primarily interact with the division of the FDA approving applications for new molecules (INDs and NDAs), I assume the regulators in the Office of Generic Drugs do not take into account branded producers' producer surplus. Since the whole point of having generic drugs is to remove monopoly profits from this group of firms, it seems reasonable that a reviewer at the OGD would not feel as if his or her job was to serve the interests of branded producers.

Producer surplus among generic drug producers is also intertwined: applicant j would earn more profits on drug X if its application were approved quickly while all the other applicants for drug X experienced very slow approval times. Since all applicants would like their own application to be approved faster and others approved slower, the aggregate producer surplus effects cancel each other out in the case of symmetric firms. However, larger firms with more drugs in their portfolio, employment, and sales are likely to have more political clout and may be able to speed their own applications in an absolute sense, or relative to others. I use the variable *Parent Portfolio Size* to proxy for the size and importance of the parent (or the firm, in cases where there is no parent). These larger firms are repeat and frequent players in interactions with the agency and important constituents for elected representatives who ultimately oversee the agency. Large generic manufacturers have influence with their legislators due to substantial employment in a local area, for example, while parent firms often have high political profiles, lobby government officials regularly, and contribute to political campaigns. If the FDA wishes to please large and powerful firms, applications with high parent or firm portfolio size will be approved quickly.

I also construct a variable, *Brand*, which indicates that the firm primarily submits NDAs rather than ANDAs: a majority of its activity is as an innovator. The FDA could have more scientific confidence in the products of innovator-owned firms or might feel more pressure from their multifaceted and well-developed relationships with the FDA.

Both the FDA and the producers can see the order of entry into a particular drug compared to the order of finishing after several applications have been approved. For example, a firm could see that its application was the second to be received by the FDA for a particular drug, but was the sixth to be approved. It is likely that the applicant's regulatory affairs manager will suffer from this sort of bad relative performance and has an incentive to complain to the agency about the firm's review experience.[10] This might lead reviewers to try to preserve the order of applications as a way of reducing complaints. In this case the agency can take longer to approve an application with a substantial head start over its next rival in the same market - because original ordering will be preserved - without generating too many

[9] Using the same framework as the consumer surplus example, the additional producer surplus is $(a-c)/(n+1)^2$.

complaints. We should see those applications with another ANDA close behind being approved more quickly than an application with a long lag before the next application in that drug. *Headstart* is defined to be the number of days between a firm's submission of the ANDA and the next firm's submission of an ANDA in the same drug market. *Headstart* is undefined for the application submitted latest in each drug market.

It may also be the case that producers succeed in influencing the agency by affecting the utility of the bureaucrats in the agency more directly. Bribing bureaucrats was one method that firms did try to gain themselves advantage. The variable *Bad* is defined as in previous sections: it is one if the firm was later indicted in the scandal. *BadBehind* is a dummy variable that takes the value one if the firm submitting after the firm of interest was indicted in the generic scandal. The idea is that the bad firm is bribing the FDA to push its application through faster, but the FDA does not want to change the order of applications. Therefore, the application ahead of the bad one will be approved faster also (thereby defeating part of the purpose of the bribing firm). *BadBehind* is always zero if the submission is before patent expiration because the time pressure on the agency is much weaker. *PPSBehind* is the analogous variable constructed using *Parent Portfolio Size*. If there is a politically powerful firm behind the application of interest, that application may be approved faster.

I define *Early* to be the number of days before patent expiration an application is submitted. A submission after the patent expires produces a negative value for *Early*. In calculating *Early*, patent expirations before the regulatory change on November 1984 are set to that date. An ANDA could not have been submitted any earlier than November 1984. The mean value of *Early* is -374, indicating that the average application is submitted about one year after the relevant patent expiration. The negative mean is partly a regulatory phenomenon. In the first years after Waxman-Hatch there was a rush into underserved markets where patent protection had already expired, and all of those entrants were late by the definition above. The mean value for *Early* for drugs with patent expiration dates in 1987 or later (submitted before the scandal) is 320 days. Firms were still overly optimistic about the regulatory process as the mean approval time for this group (before the scandal) was 393 days.

ANDAs that are submitted before patent expiration must be analyzed differently from those that are submitted 'late.' The FDA may not be in such a hurry to approve an application if the FDA's decision is not the binding constraint preventing consumer surplus from being realized. In other words, an application that is submitted sufficiently early (relative to patent expiration, not relative to competitors) can move through the process slowly and still be approved before the relevant patent expires, or soon

[10] FDA resources that determine overall mean approval times are not under the control of anyone outside the FDA

thereafter. It is also the case that a firm is more likely to submit an application early when it expects a long approval time. *Early0* is equal to the *Early* variable in the positive range, but takes on a zero value whenever an application is submitted after patent expiration. The *Early0* variable measure the number of days of "slack" that the FDA has available before its delay starts causing consumer and producer surplus losses and is also a proxy for application quality.

The applicant's level of experience with the drug or form lowers its cost of creating an ANDA with characteristics that match those of its existing portfolio of drugs. This experience may be capturing a 'capability' of the firm's research team that allows the firm to create an application of higher quality. I create several variables that measure whether the current ANDA's characteristics (drug, form, and therapeutic class) match the characteristics of any drugs in the firm's portfolio. These variables are called *Drug Match*, *Form Match*, and *Therapy Match*, respectively. *Drug Match* also includes the parent firm's experience with the drug, which is important in cases where a branded drug is 'passed' on to a generic subsidiary. In related research (Scott Morton (1997)) I show that generic firms choose to enter markets where they have this past experience. We expect to see higher quality applications in an area where the firm has a reputation already leading to quick approvals.

Other characteristics of the drug that affect approval times through capturing risk or technical features are whether it treats a chronic condition or not and the share of sales to hospitals. These two features are proxies for medical risk of the drug. A medicine for a chronic condition must be taken regularly over several years whereas acute conditions are treated in a short amount of time. Drugs with a high proportion of sales to hospitals are typically those which a patient cannot administer to him or herself (such as injectable drugs) or drugs that are especially strong (such as cancer drugs). As the FDA reviewers' become more sensitive to the risk of approving a dangerous drug, the coefficients on these variables may change. Form fixed effects are also included to proxy for technical differences across drugs. Both specifications include year fixed effects to control for variation in FDA resources relative to the tasks at hand.

Firm-specific variables are used to predict approval times, rather than using firm dummies. Firm dummies are a very crude way of getting at the effects of the portfolios, experiences, and other characteristics of the firms in the sample, especially when these other characteristics can be measured. In

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and therefore it is very unlikely a firm would evaluate a manager on absolute as opposed to relative approval times.

addition, because there are about 180 firms and approximately 320 drugs, some of which have only one observation each, the effective sample size would be much reduced by the inclusion of firm dummies.[11]

The summary statistics for the variables are reported in Table VI, in addition to other information about the firms in the sample. The variables are correlated with one another in the expected manner. The total number of entrants increases as market size (brand revenue before patent expiration) increases (ρ=0.33). The correlations between large market and early application, and large market and early approval are 0.36 and 0.33 respectively. This suggests that firms respond to the increased benefit of getting into popular, large-revenue drugs early and the FDA may be expediting those applications. Large firms are more likely to be early (ρ=0.16), which suggests they might be more professional about the application process than smaller firms. Markets with entry before 1984 tend to have lower total revenue, presumably due to the age of the market and the lower price of generic products. Not surprisingly, these markets attract fewer entrants after 1984.

We might expect a variable's effect on approval speed to differ before and after the generic scandal. More generally, the scandal likely caused a regime change. After the generic scandal, the perceived risk of approving a drug increased sharply. Firms had been caught engaged in fraudulent behavior that was dangerous to the public and every application was under suspicion. Clearly approval times should have increased if the reviewers at the FDA cared about consumer surplus or about avoiding another FDA scandal. Therefore, the specification is estimated separately on the two periods. *Bad* is not included in the second specification because firms with employees who were actually indicted in the investigation do not have any approvals after 1990.[12] The results of the estimation of Equation (2) in both samples are reported in Table VIII.

B. Results of Hazard Rate Specification

The coefficient on the variable *Bad* is consistent with the earlier OLS analysis. *Bad's* positive and significant coefficient indicates that the bribery and other illegal acts gained firms significant advantage in the approval process. An application combined with illegal tactics was more likely to be approved at any given moment than an application from an identical, but honest, firm. In addition, having such a firm submit an application just after you in your market also reduced approval times. This result is interesting since presumably the bribing firm would prefer to have jumped over the application in line ahead of it.

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[11] The instability of the coefficients is also increased. This occurs because a vector of zeros with one or two ones looks very collinear with a vector of zeros with one or two ones in different places; the two vectors have over 300 zeros in common. Therefore, standard collinearity problems start to appear when firm dummies are included with firm characteristics.

[12] The exception is Eon which was bought by its managers, changed its name to Vitarine, and continued to operate.

Order preservation suggests that the bribing firms did not bribe enough; the cost of complaints from rival firms must have outweighed the bribes in the minds of the reviewers.[13] Having a large parent portfolio or large firm portfolio does not affect the speed of approval before the scandal occurs. However, after the scandal, size of portfolio has a strong effect on the speed of approval. I suspect that large firms quickly put in place the new tests, higher standards, and improved manufacturing protocols the FDA wanted after the scandal, and therefore their applications were higher quality and approved more quickly.

The market size coefficients are positive, significant and sizable both before and after the generic scandal. After the scandal, larger markets had a much bigger impact on approval times. Firms may have submitted higher quality applications or the FDA may have been so slow in approving products that consumer and producer pressure in these markets became more important. The *Order of Entry* effects are positive, suggesting learning and risk aversion on the part of the FDA, but are not significant. Since the social surplus incentive is an opposing effect, the insignificance of *Order of Entry* is perhaps not surprising.[14]

Experience with one of the ingredients in the current application speeds the application process before the scandal. The mechanism through which past experience results in quick approval times may be a higher quality application or reputation with the FDA. Since the effect of experience disappears after the scandal, it seems more likely that the scandal destroyed firms' reputations - the FDA no longer trusted specific past experience since that could itself have been gained by fraud. The same phenomenon appears to be happening with *Form Experience*. It is insignificant (along with *Therapy Experience*) before the scandal, but slows down approval after the scandal. Surprisingly, being *brand*-owned slows down an application (p-value 9%) all else equal. The brand entrants in the sample may be less familiar with the tests and procedures involved in an ANDA, since this is not where most of their activity is. The

[13] This was a reasonable position to take since the scandal was eventually uncovered by a firm that thought its applications were not being approved as fast as competitors'.

[14] It is possible to create a structural expression for the change in consumer surplus as a function of order of entry if one is willing to make assumptions such as linear demand, constant marginal cost, and Cournot competition. In a model with linear demand and constant marginal cost c and intercept a, for example, the Cournot equilibrium price will decline from $(a-c)/(n^2)$ to $(a-c)/(n+1)^2$ with the addition of the n^{th} entrant. If instead of entry order and revenue a structural variable measuring consumer surplus is used, it has a weakly negative effect on the probability of approval. The change in consumer surplus as the number of entrants changes is: $dCS/dn=[(a-c)/2]*[((2a-c)n+c)/(n+1)^3]$, so I use $n/((n+1)^3)$ as an approximate derivative of consumer surplus without the market size terms. To account for market size in the absence of marginal cost and demand parameters, I use the log revenue of the market. *Consumer Surplus* is defined to be *LnRevenue* times this approximate derivative. In various specifications it has either an insignificant or positive effect on the length of approval times. These results run counter to the consumer surplus theory. The results therefore provide no support for FDA response to structural measures of consumer surplus; the FDA may in fact, not care about consumer surplus, or the measurement method employed here may be incorrect.

disadvantage disappears after the scandal, which may be attributable to brands having better reputations for quality within the FDA.

Having a substantial *headstart* before the scandal causes slower approval as the FDA uses up the slack time, although the p-value of the coefficient is only 7%. This effect disappears completely after the scandal. More detailed and stricter procedures on how to process applications took effect after the scandal and resulted in much less discretion for reviewers. *Early0* is strongly significant; the earlier an application is submitted, the longer it takes to be approved. The agency may be using up slack time where consumer and producer surplus would not be lost due to delay, or firms may be intentionally submitting early applications where a long approval time is expected. The post-scandal results provide support for the former explanation because the priorities of the FDA changed sharply and firms could not have quickly adjusted by submitting *different* applications early.

Markets with a high share of sales to hospitals appear to be approved much more slowly after the generic scandal, while controlling for drug form. These drugs are likely to be stronger and potentially more dangerous. Chronic drugs are also approved more slowly after the scandal hits. The FDA's new attitude toward risk may be showing up here. In general, markets with entry before 1984 do not appear to be significantly different from other markets. Both a dummy coefficient (specification not reported) and interaction of the dummy with order of entry, fail to significantly affect the probability of approval. The coefficients on the year fixed effects, though not reported, continue to displaying the pattern revealed in Table VI.

8. Conclusions

The generic scandal of 1989 is clearly visible in the descriptive statistics of approvals and application times. The illegal behavior generic firms engaged in appears to have had a negative impact on time required for approval of a generic drug, - about nine months on average - although the estimated coefficient only reflects illegal behavior subsequently uncovered. Applications submitted by indicted firms could represent less or more than the full set of illegal activity. Additionally, bribes appear not to have been effective enough to cause the bribing firm to jump a place in the queue. Instead, the application in front of the bad application was pushed through faster than normal. This indicates that the bribes were not entirely effective at changing relative performance.

There is a large amount variance in approval times both across and within drugs and firms. Dummy variables for drug, year, and firm can explain about 40% of the variance in approval times; therapeutic class and form variables do not explain significant variation. Firm effects are significant,

indicating that some firms in the sample consistently submitted applications that were approved quickly (without bribes) and others appear to have lacked this crucial skill.

In both regimes the FDA is quicker with applications for large revenue markets. However, this is not evidence of a concern for consumer surplus as application quality and producer surplus also increase with the size of the market. A negative coefficient on *OrderOfEntry* would provide evidence of FDA concern for social surplus. However, *OrderofEntry* is insignificant in both regimes. It appears that organizational learning about a new drug and delay due to caution in the face of a new product counteract the effect of the agency's concern for consumer and producer surplus.

Agency resources clearly affect approval times; this appears in the year effects after the generic scandal (much slower) and in the agency's use of slack provided by applications submitted before patent expiration. The FDA seems to use extra time to minimize complaints and political hassle from constituent firms. For example, the agency uses up a firm's head start over rivals instead of changing ordering to save itself complaints from generic firms. The *headstart* effect disappears after the scandal when strict procedures for processing applications were put in place and discretion was greatly reduced. *Early* applications, those submitted before patent expiration, also take longer to approve, both before and after the scandal, which indicates the FDA is using the available slack in the system. The political power of large generic firms does not seem to reduce their approval times, at least before the scandal. However, large applicants (measured by portfolio size) do receive approvals quicker than small applicants after the scandal.

Several aspects of the results indicate that the FDA is concerned with consumer safety. Drug-specific experience enhances both a firm's reputation and the quality of its application and helps firms get approvals quicker before the scandal. After the scandal, the FDA becomes more sensitive to risk. More dangerous hospital-administered drugs and regularly-taken chronic drugs take longer to gain approval. Also, drug experience no longer has any effect on approval time. Because of all the fraud that had occurred in the past, the FDA no longer values past experience with the drug. Overall, the results provide most support for an agency responding to bureaucratic preferences, complaints from constituent firms, and risk to consumers, rather than one trying to maximize classic measures of social surplus (absent risk considerations).

References:

Baron, David and David Besanko (1984) "Regulation and Information in a Continuing Relationship," *Information Economics and Policy:*267-302.

Bosch, Jean-Claude (1994) "Wealth Effects of Food and Drug Administration (FDA) Decisions" *Managerial and Decision Economics*:15:6:589-599.

Dranove, David and David Meltzer (1994) "Do important drugs reach the market sooner?" *The RAND Journal of Economics*:25:1:402-423.

Joskow, Paul (1974) "Inflation and Environmental Concern: Structural Change in the Process of Public Utility Price Regulation," Journal of Law and Economics

Kaitin, K. et al (1991) "Therapeutic Ratings and End-of-Phase II Conferences: Initiatives to Accelerate the Availability of Important New Drugs" *Journal of Pharmacology*:31:17-24.

Niskanen, William (1971), Bureaucracy and Representative Government, Chicago, Aldine-Atherton.

Noll, Roger, et. al. (1973) "Economic Aspects of Television Regulation," Brookings Institute.

----, (1985) "Government Regulatory Behavior: A Multidisciplinary Survey and Synthesis" In R. Noll (ed.) Regulatory Policy and the Social Sciences, Berkeley, Univ. of California Press.

Olson, Mary (1995) "Regulatory Agency Discretion among Competing Industries: Inside the FDA," *Journal of Law, Economics, and Organization*:11:2:379-405.

----, (1997) "Firm Characteristics and the Speed of FDA Approval," *Journal of Economics and Management Strategy* :6:2:377-401.

Quirk, Paul J. (1980) "Food and Drug Administration" in The Politics of Regulation, James Q. Wilson ed., Basic Books Inc., New York.

Quirk, Paul (1981) Industry Influence in Federal Regulatory Agencies, Princeton University Press, Princeton, NJ.

Stigler, George (1971) "The Theory of Economic Regulation," *Bell Journal of Economics*, Spring 1971, pp2-21.

Stigler, George (1972) "The Process of Economic Regulation," *Antitrust Bulletin* 17:207-236.

Weingast, Barry and Mark Moran (1983) "Bureaucratic Discretion or Congressional Control: Regulatory Policymaking by the Federal Trade Commission," *Journal of Political Economy*:91:765-800.

Zarembo, John E. (1991) "Individual Report: Fairness in FDA's Generic Drugs Program," from Hearings Before the Subcommittee on Oversight and Investigations of the Committeee on Energy and Commerce, U.S. House of Representatives, *FDA's Generic Drug Enforcement and Approval Process*, March 7 and June 5, 1991

Table I: Applications by Year of Submission and Year of Approval*

appvd: submit	84	85	86	87	88	89	90	91	92	93	94
84	0	23	39	17	5	0	0	1	0	0	0
85	\	38	147	77	26	7	2	2	1	0	0
86		\	60	159	92	17	4	7	2	7	0
87			\	30	164	32	6	5	6	2	0
88				\	14	49	18	46	19	9	2
89					\	0	2	24	34	15	9
90						\	0	2	21	20	5
91							\	0	14	21	18
92								\	1	23	37
93									\	3	15
94										\	1

* Year of approval is replaced by year of tentative approval when it exists.

Table II: Applications by Year of Submission and Form

	total	pill	extended release pill	injectable	topical	other oral	eye	aerosol
84	85	65	1	11	2	4	2	0
85	300	157	8	88	18	23	6	0
86	348	205	7	87	13	33	2	1
87	245	139	4	62	15	25	0	0
88	157	93	3	27	15	15	4	0
89	84	44	0	24	5	10	1	0
90	48	26	1	6	5	8	2	0
91	53	34	0	10	5	4	0	0
92	61	31	2	9	4	5	10	0
93	18	9	0	2	0	5	2	0
94	1	0	0	0	0	0	1	0

Table III: Approval Time Summary Statistics
(measured in days)

Approval Year♦	Obs	Mean	Std Dev	Median
All Years	1399	613.8	417.8	486.8
84 submitted	85	611.2	349.6	
85 submitted	300	516.0	351.4	
85 approved	61	233.3	88.3	
86 submitted	348	542.9	439.2	
86 approved	246	351.1	152.5	
87 submitted	245	464.6	344.6	
87 approved	283	450.7	204.7	
88 submitted	157	820.3	480.5	
88 approved	301	528.5	268.2	
89 submitted	84	1128.7	336.7	
89 approved	105	599.4	295.1	
90 submitted	48	947.4	257.4	effect of generic
90 approved	32	930.6	403.3	
91 submitted	53	763.9	253.3	scandal in these
91 approved	87	1120.5	341.0	
92 submitted	61	556.0	173.2	years
92 approved	98	1025.8	436.4	
93 submitted	18	380.2	164.0	
93 approved	100	1051.5	624.9	
94 submitted	1	273.6	.	
94 approved	87	884.6	482.4	

♦Where it exists, tentative approval year is substituted for final approval year.

Table IV: ANOVA of Approval Times♦

	1			2			3		
	SS	%TSS	F	SS	%TSS	F	SS	%TSS	F
year	23097	.094	18.62*	12821	.053	12.36*	13992	.057	13.37*
drug	57832	.237	1.44*	49100	.201	1.46*	50400	.207	1.49*
form	3452	.014	5.57*	903	.004	1.74	911	.004	1.74
therapy	302	.001	1.22	320	.001	1.54	326	.001	1.56
firm	--	--	--	38622	.158	2.26*	---	--	--
parent	--	--	--	--	--	--	35743	.147	2.37*
unexplaind	131247	.538	--	92625	.594	--	95447	.391	--
model	112852	.462	2.67*	151473	.406	2.89*	148521	.609	2.93*
Total	244099	1	--	244099	1	--	243968	1	--
Adj. R^2	0.289			0.406			0.401		
N	1399			1399			1398		

* denotes significance

♦ While there are 36 therapeutic classes in the dataset, only two are unique when drugs, forms, and firms can explain variation.

Table V: OLS Analysis of Approval Times with Attention to Firm Coefficients

Dep. Var.: Approval Time		(1)	(2)	(3)	recd<87 apvd<90
Year	1985	-179.2	-137.6	-129.3	-99.4
		(40.6)	(37.9)	(38.0)	(34.1)
	1986	-99.4	-94.4	-82.7	-121.6
		(43.9)	(40.4)	(41.3)	(36.2)
	1987	-146.1	-142.6	-128.3	---
		(46.0)	(42.1)	(42.8)	
	1988	141.2	127.0	145.0	---
		(55.1)	(54.7)	(54.3)	
	1989	413.8	377.8	401.5	---
		(61.3)	(65.1)	(64.6)	
	1990	203.9	147.4	179.1	---
		(74.0)	(74.3)	(73.8)	
	1991	12.5	-28.0	-1.82	---
		(70.0)	(80.4)	(79.0)	
	1992	-236.0	-253.0	-229.2	---
		(68.7)	(81.7)	(80.9)	
	1993	-395.8	-443.1	-436.0	---
		(99.6)	(104.5)	(105.4)	
Form	Inject.	201.3	107.0	---	---
		(53.4)	(75.8)		
	Topical	284.6	232.0	---	---
		(124.2)	(107.5)		
	Oral Liq	207.8	108.0	---	---
		(57.2)	(54.3)		
	Eye	335.3	390.5	---	---
		(172.1)	(241.2)		
	Ext. Rls Pill	138.7	214.7	---	---
		(88.4)	(111.7)		
Bad	---	---	---	---	-272.5
					(109.8)
Drug Dummies		yes	yes	yes	yes
Firm Dummies		no	yes	yes	yes
Parent Dummies		no	no	no	no
Therapy Dummies		yes	yes	no	no
Adjusted R^2		0.289	0.406	0.403	0.348
Observations		1399	1399	1399	705

Analysis of specific coefficients from Column (2)

Most negative *Firm* coefficients (fast)*:
-627 (151) Westward
-574 (281) KV Pharm
-561 (310) Alcon Labs
-544 (185) Reid Row
-522 (106) American Theraptcs.
-519 (136) Thames Pharma
-518 (137) Adria
-506 (138) Charlott
-510 (138) Lannett
-498 (141) Naska Pharma

Most positive *Firm* coefficients (slow)*:
1462 (160) Liquipharm
730 (254) Mikart
{635 (695) G.C. Hanford}
484 (216) Bedford Labs
471 (156) Topiderm
458 (156) Cetus Ben Venue

Therapy Coefficients:**
+252 (176) anti-infective
-421 (92) anti-hypertensive

* The firm's coefficient, measured in days, is reported followed by its standard error in parentheses. Coefficients are only reported for firms with more than one application in the dataset; systematic speed or delay being more indicative of a firm's capability or lack thereof, or improper behavior. The omitted firm is ABIC which has a mean approval time of 700 days. ** only therapeutic classes from column (2) regression with drug fixed effects. *** regression not reported, but discussed in the text. The omitted form is a pill. The omitted therapeutic class is analgesics.

Table VI: Firm Activity and Summary Statistics
(* denotes employee(s) found guilty in scandal)

	Obs	mean	std dev	min	max
Applications per drug since 1984	1399	7.26	5.19	1	23
Applications per drug* including portfolio data	1399	8.02	5.72	1	25
Firm Applications since 1984	1399	28.9	19.6	1	65
Firm Portfolio Size	1399	45.0	35.2	1	125
Parent Portfolio Size	1399	60.6	49.2	1	219
Order Of Entry	1399	5.24	4.30	1	25
LnRevenue	1360	10.14	1.80	-0.693	13.3
Brand	1399	0.084	0.278	0	1
Average Firm Time	1219	574.8	259.2	60.8	2555
Firm+Parent Experience	1399	0.841	2.18	0	23
Firm Drug Experience	1399	0.613	1.53	0	18
Parent Drug Experience	1399	0.228	1.26	0	18
Bad	1399	0.183	0.387	0	1
Headstart	976	238.8	343.1	0	2859
Early	1392	-369.8	741.4	-3346	2920
AprvdEarly	1392	-982.7	855.0	-3620	2524

10 generic firms with highest # applications (estimable observations only):

Geneva: 65	PBI*: 57	Danbury: 52	Barr: 49	Roxane: 41
Quad*: 59	Mylan: 56	Lemmon: 50	Par*: 46	Lyphomed: 40

Drug categories (all forms) with highest # applications (estimable observations only):

Metoclopramide 33	Haloperidol 24	Indomethacin 20	Clindamycin 19	Cephalexin 18
Propranolol 31	Diazepam 21	Albuterol Sft 19	Lorazepam 19	Verapamil 17

Firms or Employees Implicated in Scandal:	Par Quad Vitarine/Eon Superpharm Quantum Pharmics PBI Bolar American Therapeutics Chelsea

Number of Firms active (submitting ANDAs) in a given year:

1984:34	1986: 93	1988: 54	1990: 30	1992: 27	1994: 1
1985: 80	1987: 79	1989: 39	1991: 29	1993: 10	

Table VIII: Hazard Rate Analysis of Approval Times*

Dependent Variable: Approval Time	Sample is Approvals Before Scandal (1984-88)	Sample is Approvals After Scandal (1989-1993)
Bad Firm	.267	---
	(.094)	
Bad Firm in Application Behind	.197	---
	(.096)	
Parent Portfolio Size	.0012	.019
	(.0013)	(.004)
Parent Portfolio Size of Application Behind	-.0004	.0025
	(.0008)	(.0020)
LnRevenue	.090	.292
	(.035)	(.106)
Order of Entry	.0095	.008
	(.0094)	(.049)
Experience with Drug	.036	-.017
	(.020)	(.069)
Firm Experience with Therapy	.0054	.019
	(.0090)	(.025)
Firm Experience with Form	-.001	-.015
	(.002)	(.006)
Brand-owned Firm	-.157	-.068
	(.092)	(.243)
Headstart	-.00021	-.0002
	(.00012)	(.0004)
Early0	-.00045	-.0016
	(.00017)	(.0004)
Share Hospital	-.019	-1.64
	(.118)	(.412)
Chronic	.018	-.359
	(.081)	(.237)
Form Dummy variables?	yes	yes
Year Dummy variables?	yes	yes
Observations	847	116
Log Likelihood	-4810	-378

- Cox proportional hazard model. Standard errors in parentheses.

Figure 1: Hazard of Approval, Pre-scandal sample, 1984-1988

Figure 2: Hazard of Approval, Post-scandal sample, 1989-1994