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Application: NBER Innovation Policy Post-Doctoral Fellowship

January 2, 2014

It is my pleasure to submit my application for the NBER's Innovation Policy Post-Doctoral Fellowship.

I am interested in the intersection of innovation policy and the economics of health care, including incentives for innovators, producers, and consumers of new medical technologies, the effects of policies that regulate innovation on public health, and the relationship between innovations in medical technology and cost growth in the U.S. health care system.

I graduated from Dartmouth in 2005 with a major in Economics. For my thesis, I was awarded the Haney Prize for the best honors thesis in the economics department. I have been a PhD student at Harvard since 2009, where my coursework has included advanced econometrics, health economics and public finance, with supplementary cross-registered coursework at MIT in the Economics of Ideas Innovation and Entrepreneurship and at Harvard Business School in Innovation in Healthcare. I will be graduating in May, 2014.

My job market paper, which I will continue to work on over the coming year, considers innovation incentives in medical technology. In particular, I ask the question: does the regulatory system in place create advantages or disadvantages for pioneer medical product innovators?

When does regulation help or hinder pioneer innovators? On the one hand, first mover advantages in commercializing new technologies arise when firms can capture substantial market share, for example through exclusive patenting. On the other hand, early innovators may pay large fixed costs in order to establish regulatory precedents and in doing so, allow subsequent entrants to free ride. Thus, the effect of novelty on pioneer innovators is ambiguous.

Industry regulation, in turn, is often associated with delayed or reduced firm entry; all else equal, extended time between a new invention and its commercialization will reduce incentives to innovate. For example Roin et. al. (2013) find evidence of this phenomenon in cancer research and development (R&D). Reductions in firms' innovation incentives will have a downstream effect on their strategies for entering new markets. My paper explores one determinant of these market entry choices by considering the costs of being a first mover innovator in the context of new medical product regulation in the United States.

In the United States, all medical technologies are regulated by a single agency, the U.S. Food and Drug Administration (FDA). The FDA regulates two trillion dollars worth of products every year, including 80 percent of the U.S. food supply, cosmetics, animal products, and, importantly for this study, all ethical drugs and medical devices (Babiarz and Pisano, 2008). The FDA also regulates several emerging classes of medical products such as biologic drugs ("biologics"), nanomedicines, tissue engineered products, and the use and applications of cellular and gene therapies.

Previous studies of medical innovation under FDA regulation have focused on the pharmaceutical drug industry (Goldman and Lakdawalla, 2012), where early mover regulatory advantages have been documented. For example, Carpenter et. al. (2010) find a small but statistically significant relationship between entry order into a drug market and approval times for new drugs: going from being first to second in a given market is associated with just over a week longer spent in regulatory approval (approximately a 1.2 percent increase in the length of the approval process). However, newer classes of medical technology are characterized by a larger degree of product heterogeneity and significant regulatory uncertainty, changing the context of new product regulation.

I begin by comparing the dynamics of the well-established regulatory approval process for new chemical drugs to the less studied and more uncertain regulatory approval process for

new medical devices, a category including products as wide-ranging as pacemakers, coronary artery stents, and silicone breast implants. I find that, in contrast to the early entrant advantages observed in drug regulation, first movers in medical device markets experience a strong disadvantage in the regulatory approval process. Using data spanning three decades of regulatory approvals (1977-2007), I show that pioneer entrants in new device product categories spend 34 percent (7.2 months) longer in the approval process than the first follow-on innovator in that category. This represents 16 percent of the total period of market exclusivity a pioneer device innovator can expect to experience. Given the concentration of earnings in the earliest years a device is on the market, back-of-the-envelope calculations suggest that a delay of this length could mean a loss of approximately 8 percent of expected lifetime product revenues.

I then ask how different types of regulatory uncertainty are related to approval times in the medical device setting. I first consider technological uncertainty – uncertainty on the part of the regulator that involves a lack of scientific understanding of a specific type of product, which is used for a given function in the human body. Technological uncertainty arises most frequently in the evaluation of very novel medical devices, where the regulator needs to understand the scientific mechanisms through which a device works in the human body. Consider for example the first time that the FDA was asked to evaluate an implantable cardioverter defibrillator (ICD[1]) for approval. The FDA approved the first ICD in 1984 and at that time, the specific technological uncertainty faced by regulators was centered around understanding precisely how the device interacts with the heart and the surrounding tissues with which it is in contact.

Research and development on ICDs continued over subsequent years and to date, over two dozen later-generation ICDs have been approved by the FDA. Some of these ICDs were classified under the same product code as the originally approved device, but starting in 1997, some approved ICDs were given a new product code due to modifications in the design of the device (for example, one group of ICDs that has emerged since 1997 involves two electrodes inserted into the heart, rather than just one). While these later products are somewhat different than earlier models, the FDA had already established a firm understanding of how ICDs function and how to assess the technology involved in these devices by the time that later-generation ICDs began applying for regulatory approval. Exploiting the fact that some products with the same technical function are given a new nominal classification as a result of design changes, I find that the regulator's familiarity with the primary technology used in a new medical device does not explain the length of the regulatory approval process. That is, the first ICDs in later-established ICD product codes still experienced a regulatory delay associated with being the "first entrant," despite the fact that the regulator was already familiar with the technology used.

I next consider procedural uncertainty. Procedural uncertainty occurs in the absence of clear procedural guidelines for evaluating a new product, leading to uncertainty on the part of the regulator as to how to evaluate the results of clinical studies and other (e.g. biocompatibility and engineering) tests. This type of uncertainty almost certainly co-occurs with technological uncertainty for new products, and without the establishment of clear evaluation standards, it will persist long into a product's development lifecycle. Procedural uncertainty is easiest to think of in a scenario in which a product and its functionality are known to the regulator, but evaluation criteria are not standardized or formally established. This occurred in the case of drug eluting

[1] An ICD is a small device that is surgically placed in the chest or abdomen, which is used to treat irregular heartbeats called arrhythmias. An ICD uses electrical pulses to help control life- threatening arrhythmias.

stents[2] (DESs), which were first submitted to the FDA for approval in 2002. It was not until 2008, however – after five different DESs had submitted applications for regulatory approval and four had already been cleared – that the FDA published a formal guidance document, detailing what criteria it would use to make approval decisions about DESs moving forward.

With this in mind, I consider the release of FDA guidance on DESs and eight other medical devices. In each case, objective regulatory guidance was introduced for a group of already-established products (i.e. multiple approvals had already occurred). I find that on average, approval times for subsequent entrants fall by approximately 40 percent (6.1 months) for these nine products after application content and evaluation procedures are made explicit through formal guidance. In contrast to technological uncertainty, procedural uncertainty appears to play a large role in explaining regulatory approval times for first movers, and overall.

This finding has implications for other emerging categories of medical technology including biologics, tissue engineered products, and the applications of cellular and gene therapies – all settings with a large degree of procedural uncertainty around how to evaluate new products due to a lack of established regulatory criteria. For these new product categories, regulatory approval times are similarly likely to be substantially protracted (relative to what is administratively required) until a time when objective evaluation criteria are established.

After showing the impact of uncertainty on review times, I consider how the implicit costs of the regulatory approval process affect firms' strategies for entry into new medical device product categories. I consider firm behavior under regulatory uncertainty, given likely (additional) costs of gaining regulatory approval in new markets. I evaluate the behavior of all cardiovascular device firms in the data and find that financially constrained firms are less likely to enter new device markets as pioneers: the fraction of financially constrained firms among pioneer entrants into device markets is 25 to 52 percent lower than among follow-on entrants.

My current research has illustrated crucial differences between the regulatory approval process for drugs and devices, and I hope to next explore in detail how firms strategically approach the medical device regulatory approval process. In particular, I am interested in whether firm size and financial constraints play a role in determining timing of firm entry into new markets, and how firm characteristics are related to the probability of successful product commercialization. To fully understand the development lifecycle of new medical devices, I have requested data from the FDA on the early-stage Investigational Device Exemptions (IDEs) that grant permission for devices to be used in clinical trials. I hope to identify determinants of both successful IDE applications as well as success in the subsequent Premarket Approval (PMA) process for medical device firms.

I look forward to continuing my research and know that my projects would benefit greatly from the support of the NBER's Innovation Policy Post-Doctoral Fellowship. In particular, I would be very eager to learn from the community of innovation policy scholars at the NBER and also know that the working group activity-planning component of the role would be of high relevance to my research as I continue to get to know both the literature and academic community in the economics of innovation. I believe that my academic background and track record of producing high quality research make me an ideal candidate and I look forward to hearing from you.

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[2] Stents are small metal tubes that are inserted and expanded into the artery wall and used to keep the previously narrowed artery segment open. Drug eluting stents (DESs) are medication-coated stents that reduce the chance of renarrowing of the blood vessel (Maisel and Lasky, 2007)