Abstract

Regulatory policy on medical technology is an important force behind the internationalization of trade with medical devices, product markets, and regulatory issues. Both the FDA and EMA (European Medicines Agency) play crucial roles in regulating medical products, but from a comparative perspective the FDA is unique. It is the oldest and most independent regulatory agency, and has tested experience and a world-wide reputation. Because of these factors, what the FDA does, how it views the universe of medical technologies, and the mechanisms it adopts, as well as how it sets enforcement trends, are of key interest to stakeholders from all corners of the globe.

Examining the developing literature on regulation and governance, a key contribution is the book by Daniel Carpenter, Theory of power and reputation: organizational image and pharmaceutical regulation at the FDA (2010). An important question is can it satisfactorily explain the performance record of the FDA in the medical device sector? An answer demands both the gathering of empirical data and a critical examination of four inter-related dimensions: (i) an examination of the role of the FDA as a defender of public health; (ii) its historical-political role over forty-five years; (iii) an identification of the FDA’s policies and politics (executive, business, and professional/scientific) in the device sector; and finally, (iv) a critical examination of the FDA’s approach of relying on currently satisfactory devices as a basis for assessing the safety and effectiveness of new high-risk devices, not only moderate-risk devices. Using empirical data from the medical device sector, we may be able to provide an alternative theory and interpretation.
The primary reason for writing this paper on the FDA is the manifest contradictions between the well-established reputation and power of the FDA, on the one hand, and the rising criticism of the FDA’s performance in the field of medical devices over the last decade, on the other. Contradictions and puzzles follow from an initial review of a host of primary and secondary source materials consulted for this paper. The sample of brief article headings below gives a taste of the scope of regulatory issues as well as the dark side of medical device regulation: Many patients are hurt or disabled for a lifetime, or they die due to a defective implant, or because something went wrong in surgery or post-surgical treatment.

- “Bad Wire in Heart Device Led to 22 Deaths, Study Says” (Thomas 2012).
- “Study is Ended as a Stent Fails to Stop Strokes” (Kolata 2011).
- “IOM report recommends abandoning US FDA 510(k) in favour of new framework, industry concerned” (Sharma 29 July 2011).
- “Experts Oppose Metal-on-Metal Hips” (Meier 03/14/2012).
- “Implant at Own Risk” (Meier 04/03/2012).
- “Remedy is Elusive as Metallic Hips Fail to Fast Rate” (Meier 2011).

Moving towards the delivery of health care a grimmer view still emerges. A patient suffers from radiation overdoses due to an equipment failure. An operating table collapses, a syringe is disconnected. Pain management equipment does not deliver the pain medication it is designed to. The trigger for concerns about heart defibrillators was the revelation that Guidant Corporation did not inform patients, nor at first physicians, of defective malfunctioning defibrillators, which involve the risk of death or serious injury (Maisel 2005; Maisel 2008; Maisel and Kohno 2010; Dhuva, Bero and Redberg 2009). The guidelines of who (hospital management or surgeon) should report an adverse event, to whom they should report it (the regulator or solely the company) and when, are still not as clear as they should be. Nor is it obvious what event qualifies as an adverse event. There are many more reports, studies and media articles – not yet fully analyzed – which signal complex regulatory issues behind these patient stories and justify various narratives about the ethical, legal, economic, and political issues involved in regulating medical devices.

This first draft of on-going research is limited in scope and focuses on the most distinctive features of medical device regulation, such as risk classification, the 510(k) approval process, and what to do about them. Among the targets of serious criticism are the 510(k) procedure, which has attracted most disapproval for the ease with which even some high-risk medical devices (e.g., stents, defibrillators, and select implants) have reached the market after receiving accelerated approvals with neither a full scrutiny of the safety and efficacy of these devices or clinical trial evidence. While exact figures vary according to the source consulted, the Institute of Medicine (IOM) confirms that more than 80% of all devices since 1976 were approved through this process.
Medical device regulation in the United States spans more than forty years, ranging from pre-market notification to post-market surveillance and adverse event reporting across an expanding set of complex scientific and regulatory issues. The narrative begins with the first authorized legislation in 1938, to the Medical Device Amendments of 1976, which established a medical device structure separate from drugs, to the recent amendments in 1990 and 1997, and again in 2000 and 2007. The amendments in 1990 and 1997 were primarily concerned with clarifying the conditions for pre-market clearance, the submission of clinical studies and data to support applications for market approvals \textit{ex ante}, and the requirements for adverse event reporting by health facilities \textit{ex post}. The Medical Device User Fee and Modernization Act of 2002 was a response to the chronic underfunding of the medical device unit within the FDA. The Act introduced user fees to hire additional staff and speed up review times. User fees were extended by the Food and Drug Administration Amendments Act of 2007. The FDAAA will be extended by the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA).

Human tragedies and health disasters preceded discussion, action, and final authorization of congressional acts on drugs (Carpenter 2010; Angell 2004 and 2010; Hawthorne 2005). Did the same factors trigger the separation of medical devices from pharmaceutical regulation in 1976? Did accidents or injuries as a result of faulty devices prompt action? Or did lobbying by a newly emerging and young med-tech industry, which has carefully managed to stay under the radar screen of the media for quite some time, and related political dynamics, explain the initiation and historical path of medical device regulation over time? What did Congress hope to achieve and what were the determining factors of its action? While we will have to wait until research is completed, this much is known: The legislative amendments in the early 21st century seem to be responses to the industry’s demands for “least burdensome” regulation and the desire to promote the international competitiveness of the US med-tech industry rather than by a focus on safety and effectiveness, and risks and benefits of new devices. Moreover, the location of the industry and the electoral districts of senators and members of the House and their voting pattern for industry-friendly amendments seem to correlate.

The balancing act between innovation and commercialization of medical devices (ex ante) and public health and post-market safety surveillance of devices has always been delicate, but the rapidly growing markets of the last decade and the increasing complexity of new technologies pose a host of regulatory challenges, and challenge the tenuous balance that has been struck. On the other hand, patients’ hope for life-saving and life-supporting therapies has not diminished. Instead, this has led to more demands for new treatments with medical devices that should and must receive fast track treatment. With medical-technology innovation, the challenges for regulatory authorities in the medical device sector have increased qualitatively and quantitatively. This leads to concerns about who is in charge, what policies secure an appropriate and effective balance between early access to the market, and the safety and effectiveness, if not efficacy, of new medical devices. For instance, in the case of orthopedic implants, only their longevity after being implanted in a patient’s body will constitute valid evidence.
To ensure the efficacy, effectiveness and safety of medical devices two options exist in theory and practice. The first option is stricter *ex ante* regulation before products are on the market and before harm is done, while the second option is lax regulation and in the worst scenario paying compensation under liability law after harm has been done. Is a choice between these two opposite poles the only option, or is it possible to find a better balance between *ex ante* and *ex post* regulation? With medical device failures now increasingly public knowledge in the United States, a consensus among patient advocates and some scientific circles seems to be emerging that an effective regulatory strategy requires striking a better balance between early market release and profits, including early availability in medical treatments but stricter *ex ante* controls, notably for high-risk devices. These advocates for stricter controls argue that the balance between these opposing positions should be informed primarily by health and patient safety, even at the risk of delaying the release of a new medical device that promises superior therapeutic treatment than that is currently available (IOM 2011a).

In sum, what does it take to successfully regulate, govern, implement and monitor regulatory decisions on medical devices at the global, the national, and local levels? What does the FDA do at home and abroad that attracts both support and critical attention? What importance should be given to the historical origin of the FDA and the subsequent integration of the 1976 medical device legislation into an established organizational context, routines, and ways of regulating, implementing, and monitoring drugs but since 1976 also medical devices? These and other issues will be addressed in this paper.

This draft is organized into seven sections. It begins with a clarification of what is meant by medical devices under American public law, including other concepts vital for this research. The second section briefly explains the methodology and data collection followed by a review of interdisciplinary literature. The third section introduces the FDA as the protector of public health in the US. The fourth section explores whether the FDA is leading or following from a comparative perspective by contrasting the FDA with the European Union regulator, and drug and device regulation. The next section analyzes the various roles and powers of the FDA and how it responds to growing criticism from a broad segment of American society. The sixth section offers insights into congressional politics and policy. A final section provides a brief historical account of the Medical Devices Amendment Acts of 1976 and subsequent amendments by examining the political and administrative processes and their rationale underlying the two pathways to market – premarket authorization (PMA) for high-risk devices in class III and the 510(k) clearance notification procedure mostly for class II and class I devices (510(k) referring to the article in the 1976 legislation) The conclusion briefly offers a few lessons learned and speaks to lessons still to be learned.

1. **What is a medical device under American public law?**
The debate whether medical devices are products sui generis that require a regulatory framework independent of the drug regulatory framework, or whether some stents and other implants should be treated like drugs and be subject to more vigorous pre-market approval procedures is an on-going debate in both the US and the EU. According to the
Federal Food, Drug, and Cosmetic Act (FFDCA), a medical device can be an instrument, apparatus, implant, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, provided it meets one of three conditions of being:

- Recognized in the official National Formulary, or the US Pharmacopeia, or any supplement to them,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purpose (IOM 2011a:16-17).

Risks are product specific or specific to families of devices Class I (low risk), Class II (medium), and Class III (highest risks) or individual high-risk devices (notably implants). This risk classification while going back to the original 1976 legislation has hardly been changed. As technology has become more complex and diversified and risks less easily predictable, the lines between the risk classes have increasingly been blurred, notably with an increasing number of so-called combination products on the market.¹

Regulation means different things to different research communities and disciplinary fields. In its crudest meaning, and following Carpenter’s use, regulation consists of “rules that are backed by the power of the FDA, intended to modify behavior” (Carpenter 2010). In addition to rules, other factors come into play, such as regulatory science drawing on law, medicine and engineering. Regulatory science is defined by the NIH as “the development and use of the scientific knowledge, tools, standards, and approaches necessary for the assessment of medical product safety, efficacy, quality, potency and performance, and the role of what is a specialized and interdisciplinary area of biomedical research than can generate new knowledge and tools for assessing experimental therapies, preventive therapies and diagnostics” (Yeo 2010; FDA 2011a).

Regulatory science is by no means objective or uncontested. Being embedded in essentially political and social processes, it is socially and politically constructed. We therefore assume that the differences in risk assessment and risk management referred to below for environmental, health and safety (Vogel 2012) are not absent in medical devices regulation in the US and the EU. On the contrary, we expect them to be very present in handling uncertainty and risks in product regulation. The issue is not that one country and its scientific and regulatory community perform better or worse; the issue is that individuals – regulators, scientists, business and others – bring different risk perceptions to the task and use whatever rules, norms, and procedures exist to confront new challenges.

¹ Of the over 8000 different types of medical devices on the market many are combinational products which experts divide into three groups: (i) a device that combines devices and drugs (e.g. drug eluting stent where the medical device is key or a prefilled syringe where the drug is key); (ii) medical devices and in-vitro diagnostics (e.g. a specimen testing device; the medical device is primary agent; or a pregnancy test where the IVD plays that role); (iii) different medical devices in which several devices are combined in one implant (e.g. implantation pump).
Regulation runs the gamut of “a comprehensive policy cycle in which regulations are designed, assessed and evaluated ex ante and ex post, revised and enforced at all levels of government, supported by appropriate institutions” (OECD 2012), like the life cycle concept underlying the regulation of medical devices. For each phase in the cycle, specific responsibilities and regulatory tasks are assigned to specific stakeholders who, in theory, are accountable for their actions, with the FDA being the ultimate decision-maker and monitor; but practice may differ.

2.Methodology and Data; and Review of The Literature.
Methodology and Data. This work in progress builds on four sources: congressional hearings, literature on medical device regulation at the FDA, as well as articles written by regulatory affairs experts in e-newsletters and cross-national research on the same topic in the European Union and Japan (Altenstetter, 2008, 2010; 2011, 2012). These are supplemented by articles in The New York Times, The New England Journal of Medicine and the Journal of the American Medical Association and other academic journals, including mass media reporting. Much of the documentation on 510(k) and PMA is written by experts in diverse fields pertinent to medical devices, and the empirical data are based on internal reports, data sets, and statistics collected by the FDA.

Review of the Literature. Unlike an extensive literature on drug regulation, the literature on medical devices hardly exists as either part of health policy research, part of comparisons of healthcare systems, or as part of health care (Marmor and Wendt 2011; Marmor, Okma and Freeman 2007). There is one excellent study on the use and distribution of medical technology in health care settings in the United States (Cohen and Hanft 2004). More is known about law (Kahan 2009), innovation of medical devices (Lobmayr 2011) medicine (as referenced throughout the draft), and business (Kruger 2005; Bartlett-Foote 1992 and 2001).

The regulation of medical devices is as much about risks as it is about markets and companies. Hence this research draws on emerging regulatory studies on the varieties of preventive governance in world risk society (Grande and Zangl 2011; Beck 2007). Ian Bartle (2008) reminds us of two important perspectives underlying risk regulation – a ‘scientific technocratic’ perspective and a ‘socio-political’ (or ‘social constructivist’/’social-psychological’) approach. Other scholars contrast and compare the varieties of risk and uncertainty across a number of sectors through a lens of

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3 David Demortain in his review of Carpenter’s book applauds him for his “untiring exploitation of archives and publications, great narrative skills, and capacity for elegant theorizing” while also raising critical issues about Carpenter’s failure to deal with the FDA’s decline of reputation in recent years, the one-sided understanding of conceptual power, and his failure to acknowledge “the variety of ways in which concepts are put in practice across the world and indeed transformed as they diffuse.” In Governance: An International Journal of Policy, Administration, and Institutions, Vol. 25, No. 2, April 2012, 347-349.
regulation and governance (Moss 2002; Levi-Faur 2012), but the medical technology sector is not among them. Most studies, including this paper, use a path-dependent interpretation and approach to analysis.

Risks are contingent on context. In his more recent study, David Vogel, a prolific writer on corporate responsibility and transatlantic comparisons establishes such context by concentrating on regulation and governance across food, environmental and health policy in the US and the EU. He highlights the deep almost philosophical but certainly cultural, political and legal differences in how regulators on both sides of the Atlantic approach risks and uncertainty, and what they do about them (Vogel 2012; Vogel and Swinnen 2011; Wiener and Rogers 2002). These differences are so fundamental in transatlantic relations and risk regulation that it should also be noted that risk regulation of medical devices in other countries, unlike the United States, is closely related to comparative effectiveness research in health care and national health programs in other countries (Franklin and Budenholzer 2009) for reasons of safety, cost containment and reimbursement. The determination of risks or benefits is carried out by distinct organizations separate from regulatory authorities. Moreover, “registries are a mandatory component of the health care system and required for all implantations of high-risk devices. In the United States, there is no national system to ensure that registries exist for high-risk devices” (Resnic and Normand 2012: 876). Patient registries are the only valid databanks for obtaining reliable clinical data for medical devices, unlike for drugs. This may give us a clue as to where American and European regulators are coming from when they confront risks and uncertainty and have to make decisions.

David Vogel explains that, for example, for environmental risks, the US side assumes that there is sufficient knowledge to predict risk and do something about it, whereas the precautionary principle preferred in Europe stresses “uncertainty, that which we do not know.” Vogel quotes from a study on environmental law: “U.S. environmental law has increasingly stressed risk assessment and cost-benefit analysis…, both of which presume that we have sufficient knowledge of how to measure risk and calculate the appropriate responses.”

“The extent to which scientific knowledge or risk assessments provide sufficient information to enable policy makers to rely on them in making decisions that adequately protect public health, safety, and environmental quality represents a critical difference between recent European and American approaches to risk management” (Vogel 2012: 276).

The single most important study on the US Food and Drug Administration is Daniel Carpenter’s *Power and Reputation. Organizational Image and Pharmaceutical Regulation at the FDA* (2010). In his over 800-page opus magnum. Carpenter, a political scientist, presents the FDA as the gatekeeper over drug manufacture and patient access to drugs, and the leading shaper of regulatory science, in the United States, including leadership in the world. His research on the FDA leaves him with two puzzles. His first puzzle asks: “[w]hy in the United States – the reputed “weak state” of the Western world, the government of what De Tocqueville, Hegel and Marx all observed as near “stateless” society, the home of big business and small government
displayed the world’s most far-reaching and stringent regulations on medicine? Why, for the most part of the twentieth century, has the FDA exercised a greater degree of formal power and informal discretion over drug development and marketing than have other national regulators”? (2010: 1). Carpenter’s second puzzle is the question why drug regulators in Australia, Brazil, China, Great Britain, India, Japan, New Zealand, South Korea, and Switzerland have copied so much from drug regulation in the United States (2010). Are the same developments observable in the device sector, and can Carpenter’s theory of the FDA help explain the role of the FDA in medical device regulation?

Carpenter’s analytical-theoretical framework is a useful reference point for this research (2010: 33-70), despite major disagreements between Carpenter and Angell (2012). In the context of a 25-page paper, and at this stage of the research, it is wise to treat his various characterizations and topics as hypotheses rather than as givens and accept them at face value as applicable to the device sector. We need to conduct considerably more in-depth empirical research before we can ascertain whether his explanation of the role of the FDA for drugs is also a good explanation for the device sector. Where this draft definitely departs from Carpenter’s intellectual ambition, which is to offer a workable theory and narrative about the FDA as regulator of drugs, is this writer’s interest in a performance analysis of the FDA – clearly a narrower focus – and a belief that broad and abstract social science concepts such as reputation and power tend to blend out, mislead, or distract from the very rationale of why the FDA-CDRH (Center for Devices and Radiological Health, the organizational unit in charge of medical devices) was assigned the responsibility to protect public health and patients against risks and harm. In addition, are reputation and power good indicators of performance when they can be used to explain anything from perpetuating the status quo to the use of an approval process, to favoring a fast track approval of devices for the market and understating concerns to secure safe and effective devices on the market? We think not. The 510(K) clearance process may have been appropriate for the technologies available in the 1970s, but are no longer for the revolutionary advances of today’s complex technologies.

3. The FDA: Protector of Public Health
The FDA is considered the protector of public health and patient safety in the United States and is an active participant in global harmonization efforts in the global markets. Domestically, the FDA is criticized for an alleged use of imperfect regulatory tools and for clearing medical devices for the market without ensuring the safety and effectiveness of products on the market (Maisel 2008; Maisel and Kohto 2010; Challoner and Vodra 2011; Cuffman and Redberg 2011; Makow 1994). Criticism of the FDA by political and congressional “audiences,” scientific/professional communities, and business, including patient advocates who testified in Congress, ranges from the contention that the FDA imposes to many stringent approval standards, thus creating entry barriers to long review times, to depriving patients of life-improving and life-sustaining medical devices and not shielding them from harm and injury (GAO 2009). If the FDA has so much reputation and power, why has it not used it to bring safe and efficacious medical implants and other devices on the market? Why has it not asked
“the right questions” about the safety and efficacy of stents and implants, according to other critics (Okie 2010; Voelker 2011; Zuckerman 2008), Zuckerman, Brown and Nissen 2011)? And, finally, why has it not carried out the mandate of the Safe Medical Devices Act of 1990 which clarified that the FDA should use its premarket approval authority for high-risk Class III devices, or reclassify them to a lower risk category. “After 35 years, the FDA has not completed the task of calling for PMAs [premarket notification] for or reclassifying preamendment Class III device types” (IOM 2011a): 2004). A good many high-risk devices have come to market with limited or no clinical data.

The FDA is a global trendsetter in drug regulation, and the US the leader in medical innovation. However, it does not follow that it is also a leader in medical device regulation and enforcement (Drezner 2007, Mattli and Woods 2009, Kahler and Lake 2009, Pollack and Shaffer 2009: 235-278). As is to be expected, the FDA’s leadership depends on who the occupant of the White House is, which majority controls the Congress, and what the Supreme Court (Korobkin 2007; Garber 2010) and state courts allow the FDA to do. We discover supporters of medical devices on both sides of the aisle in Congress. In turn, US device companies have showered members of Congress with generous cash for electoral campaigns. With few exceptions, Congress and lobbyists from different segments of the med-tech industry alike continue to push for fewer regulation, faster approvals, and the continuation of the FDA’s two –pronged approach to the market – through premarket notification (PMA) and the so-called 510(K) notification procedure (see appendix 1). They quietly concede that a few areas still need improvement and/or tailor-made regulation depending on device-specific risks. The on-going debates after the Obama Administration took office and within the FDA indicate that the current leadership under Dr. Margaret Hamburg intends to turn the FDA around (Okie 2010; Zuckerman, Brown and Nissen 2011).

4. Is the FDA leading or following?
Several answers are possible. First, rather than leading foreign regulatory authorities, the FDA tends to follow the initiatives of, for example, the United Kingdom, Sweden and Australia, to recall deficient products and stop their circulation. Aided by the information from a patient registry in orthopedics, the respective regulatory authorities recalled, for example, metal-on-metal hip implants, wires, heart stents much earlier than the FDA, before faulty implants were placed in a large number of patients. The UK Medicines and Healthcare Products Regulatory Agency (MHRA) prohibited the use of metal-on-metal implants altogether. Utilizing all tools of regulatory science (not identical with academic science in terms of influence, accountability, incentives as well as time frame, etc.), the regulators paid attention to pre-market requirements and above all post-market surveillance of clinical data in assessing potential harm and risks. In other words, they made evidence-based decisions before the FDA did. Finally, predictable contradictions flow from congressional politics and lobbying pressures.

Second, if the FDA is leading in drug regulation, as per Daniel Carpenter, why do the same countries around the globe, which eagerly and comprehensively copied the FDA model in drug regulation, not reproduce the FDA’s approach in medical device
regulation and, instead, adopt either the fundamentals of the EU approach in its entirety or some key aspects, like Japan did? Japan is not alone. Australia, China, South Korea as well as countries in South America and Central and Eastern Europe have copied from the EU legal approach to medical device regulation, including consumer safety and liability law (Hodges 2005; Nottage 2005). The FDA’s approach to medical device regulation may be uniquely peculiar. More tellingly, from a cross-national perspective the US med-tech industry is known to enjoy privileges and have a comparative advantage compared to foreign device makers abroad (Wilson 2005). A worthwhile question is whether the politics of medical device regulation in the United States is matchless when compared to the politics in the European Union and its member states and Japan (Altenstetter 2008; 2009; 2010; 2011 and draft).

Third, why do American manufacturers increasingly turn to the European Union to submit their products for market approval first before they submit them to the FDA, thus challenging a belief that the FDA is always the trendsetter? In recent years, according to the reporting by the news media and statements by AdvaMed (the medical technology industry association in the United States) venture capitalists seem to move their money away from companies based in the United States and shift their business to the European Union (Cardiovascular Business 2011) and lately to Asia. This costs jobs, R&D and clinical trials. Among the reasons for this move are the alleged “uncertainty” and “unpredictability” of regulatory decisions by the FDA, its “arbitrary style of decision-making,” the delays, and its uneven practices, including an alleged “lack of predictability, consistency and transparency” of the rules that will be applied in medical device regulation. The FDA’s ability to handle complex technologies in the future is in doubt. The FDA’s decisions not only impact upon manufacturers and scientists but above all on individuals’, life, and possibly death.

Fourth, why and how has the FDA applied a seemingly double standard between drugs and devices? The FDA has set strict rules, norms, and principles of public health and safety around the authorization and enforcement of controls over drugs, while the pathways to the market for medical devices have tended to be elastic, lax and in many cases misguided since 1976 when the Medical Devices Amendments Act was adopted. The record today shows that high-risk medical devices pose as many risks to human health and patients as drugs. “Recalls of medical implants – from heart valves and defibrillators to artificial hips – are as common as drug recalls” (Deyo 2008). Why has this double standard been tolerated for so long? Do the politics of vested interests and aggressive lobbying of device makers provide a plausible explanation?

The riddles continue. In a global context, the US and the EU regulatory frameworks for medical devices are considered legitimate and valid by various medical device communities for the evaluation of medical technologies worldwide (Kramer, Xu and Kesselheim 2012, IOM 2011b). In general terms, the differences between the US and EU approach concern the approval process, the role of government or third party certifying organizations in this process, and the respective scientific advisory system, including what is an acceptable scientific test for safety and effectiveness (IOM 2011b), including adverse event reporting (Wright and Datlof 2010). The US approach for about
80% (even up to 95% as per Kramer et al. above 852) of all devices approved over the last decades has relied on a comparison of new medical devices with current satisfactory devices on the market as a basis for safety and effectiveness (the so-called “predicates” and “substantial equivalence”). By contrast, the EU approach hinges on compliance standards (scientific/medical) as the basis for safety and performance, and uses third party certification for market approval (in EU legalese “notified bodies”). In other words, scientific standards are integrated into the regulatory framework. This co-regulation instrument was used historically in some EU member states prior to the 1987 incorporation of the EU legal approach to market approval – the basis for the first EU directive the Active Implantable Medical Device Directive (AIMDD) in 1990 and other medical device-specific directives.

The leading roles of the American and European actors in global harmonization has implications for other regulators in a globalizing and interdependent world. Yet, the most intriguing puzzle in cross-national research is the observation that, despite substantial differences in regulatory policy, institutional arrangements, and politics between the FDA’s and the EU’s regulatory frameworks, and independent of their respective approach to regulation, both frameworks have come under critical scrutiny for inadequacy, ineffectiveness and an imbalance facilitating profits and fast access to the market instead of securing patient and user safety. Do technology and science override the salience of political, legal, institutional and motivational factors? The evidence will need to be unearthed by further research.

5. The FDA: “Gatekeeper” and Judge

Broadly drawing on Carpenter’s clarifications of the role of the FDA in the drug sector, this section concentrates on policymaking at the FDA, more specifically the US FDA’s CDHR, with a focus on the scope of its regulatory powers and its gate-keeping functions. The CDRH is a key player with considerable weight in regulatory politics; is a strong lobbyist for congressional largesse; is the sole risk regulator of medical devices; and plays an important role in designing, developing and applying science-based regulatory policy in the United States, and, internationally, influencing global debates about regulatory science and its application to medical devices.

The authority of the FDA over medical devices is formidable. Medical devices, like drugs, can only be marketed and sold in the United States when the FDA has declared them to be “safe and efficacious” for their primary “intended purposes.” This is achieved through one of two established regulatory routes: (i) a premarket approval (PMA) for high-risk devices in Class III and (ii) the laxer 510(k) program. The FDA’s formal power and gatekeeper role over medical devices are not identical to those over drugs, but the scope and depth of the FDA’s regulatory powers over medical devices are as far-reaching as for drugs. Carpenter documented the FDA’s power and control over developments in the national marketplace, including its extraordinary role over global regulatory issues in the international market (USITC 2007). The FDA also exercises influence over various scientific disciplines by accepting or rejecting the scientific standards they and others use in testing, engineering, and developing, including the manufacture and use of medical devices in diagnosis and treatment. The
FDA lays down the rules for advertising and labeling. It has been instrumental for medical device manufacturers to secure important global market shares and make the industry one which is very profitable and guaranteed a more than usual rate of growth in the years to come. Like in the drug sector (Carpenter 2010: 1), the FDA’s decisions to reject applications for a PMA and/or 510(k) may mean a death sentence for a business, particularly a smaller one.

How does the FDA strike a balance between these different roles and the normative requirements of an “ideal medical device regulatory system”? (IOM 2011a: 21) The process should be based on “sound science” (21); it should be “clear, predictable, straightforward and fair” (21) and it should be “self-sustaining and self-improving” (21). “The process should facilitate innovation that improves public health by making medical devices available in a timely manner and ensuring their safety and effectiveness throughout their life cycle” (21). “The process should use relevant and appropriate regulatory authorities and standards throughout the life cycle of devices to ensure safety and effectiveness” (21); and, finally, and most importantly, the “process should be risk-based” (IOM 2011a: 21).

Although details cannot be addressed at this stage, undoubtedly, the FDA-CDHR is the principal agent of device regulation, at times an accomplice and at times an opponent of the industry. Research also reveals that the FDA is occasionally a prisoner of congressional policies and politics that impede its ability to act. Internationally, the FDA throws its weight around at global harmonization efforts by the international community of regulatory authorities. Regardless of what global harmonization of medical device regulation may mean for the international community, the FDA’s domestic activities are guided by US rules on the book, the FDA’s own rationale for regulation, and its own assessment of what science-based evidence means for U.S. scientists. This irrespective of what “good clinical practice,” clinical evidence” and good “regulatory science” may mean for the remaining members of the Global Harmonization Task Force (GHTF 2007). The US FDA has participated in it since its beginning in 1992.

Undeniably, it is tempting to generalize from the drug sector to the medical device sector, but a few distinct features and properties of medical devices – for example, risk classification and the 510(k) approval procedure for low and moderate risk devices, including some high and highest risk devices – limit generalizing across the two sectors. Extrapolating lessons from studies on the pharmaceutical sector and applying them to the device sector is ill-advised, as is equating drugs with devices (McKay 1986: 41-42; IOM 2011a; 2011b and 2010). But the argument can be made that they share the same political context. Yet, macro-institutional constellations (Jordana and Sancho 2006), public and private law, the historical trajectory as well as the political economy in the United States, it will be argued, do not generate the same political dynamics –neither internally for the FDA and CDRH leadership and staff and management and organization, nor externally in relation to Congress and lobbyists. Nor can we assume that the FDA’s relationship with foreign regulatory authorities and its role in the international realm are identical. There are distinct networks of “audiences” which crowd the political space; a diverse set of specific rules, norms and procedures
applies to each sector; and responsibilities are assigned to different organizational units within the FDA. Moreover, given the substantially different organization of drug and device regulation in the European Union (Altenstetter and Permanand 2007), the scientific advisory systems for drugs and devices do not work the same way; science is brought to bear on regulatory policy in the US and the EU differently. The value systems across the two entities are more different in the dimensions that matter for device regulation than they are alike, and decision-makers, analysts, and the public are part of this equation.

With almost daily revelations of yet another defective device hurting patients, a near miss, or an outright harm to patients, the precise role of the FDA is still unclear. Nor is it obvious whether American and foreign observers of the FDA, who may be inclined to look up to the FDA because of its record in drug regulation, would uncritically endorse the notion that the narrative written about drugs is paralleled in the realm of medical devices. At this stage of the research, the FDA emerges as having a distinct, albeit contested, performance record in one sector, but not necessarily in both. And even if it were possible to document that foreign regulatory authorities wait for FDA-led guidance, one question remains: why did these countries not adopt the FDA approach to medical device approval?

The record in American medical device regulation is not impeccable. The recent controversy between the Institute of Medicine (IOM 2011a, 2011b, 2010), the FDA (Sharma 02/22/2011), scientists4 and lobbyists (for example, the Advanced Medical Technology Association (AdvaMed) and the Medical Device Manufacturers Association (MDMA) that erupted in the summer of 2011 and the subsequent controversial debates, even attacks by segments of the medtech industry, brought to light one important message: rather than a search for better ways to secure safe devices and patient safety, power politics combined with lack of resources seem to overshadow the FDA’s activities and interactions with Congress and the industry. Ideology-based arguments overstate the positions of actors while understating the importance of better regulation. The bar in medical device regulation, if anything, can and should be raised.

6. Congress and Legislative Politics
Although the review of primary and secondary materials is incomplete, three constant themes and two variables emerge in the 35 years since the regulation of devices was

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4 Two workshops (IOM 2010 and IOM 2011b) had a wide participation of academics representing a cross-section of expertise and knowledge, staff of the FDA; industry representatives, who all provided information to the discussion, presented commissioned papers which were crucial inputs to the final report (2011a). The final recommendations were approved by the 12-member Committee on the Public Health Effectiveness of the FDA 510(k) Clearance Process. Five members had a medical degree and were currently or previously on the faculty of a medical school, three were professors of law, with one in addition a PhD in earth sciences, one held a PhD in bio-engineering one MA responsible for implant surgery. In addition, the final recommendations and the report were reviewed by 14 reviewers and experts in a variety of fields pertinent to medical devices. But, the original committee assumed furl responsibility for the final content of the report subject to the supervision by two experts (one from industry and one an academic) appointed by the National Research Council. They were “responsible for making certain that an independent examination of the report was carried out in according with institutional procedures and that all review comments were carefully considered” (2011a: viii).
separated from regulating drugs in 1976. The two variables refer first to the changing relations between the FDA to Congress in two distinct time periods: from 1976 to 1990, and 1990 to the present. The second variable is the changing content of regulation from the original 1976 legislation to more flexibility to even the principle of “least burdensome regulation” introduced by Congress in 1997 through the Food and Drug Administration and Modernization Act (FDAMA), renewed in 2002, 2007 and 2012.

The first theme is the perennial complaint about lack of funding which prevents the FDA from hiring scientific staff and engaging in all tasks necessary to secure safe devices on the market. The consequences are “high reviewer and manager turnover at CDHR, which is almost double that of the Center for Drugs and our Center for Biologics, insufficient reviewer training, extremely high ratios of front line superiors to reviewers, insufficient oversight by managers, rapidly growing work load caused by increase in complexity of the devices and the rapidly increasing overall number of submissions we receive; sometimes unnecessary or inconsistent data requirements imposed on device companies, insufficient guidance for industry and FDA staff and poor quality submission from industry” (Shuren 2011). The second theme is repeated but empty promises by the FDA leadership and device chiefs to Congress that the FDA will restore a better balance between pre-market considerations and post-market controls, including safety surveillance and vigilance (Schultz 2006). The third theme is the periodic attacks against the EU approach to device regulation. This was noted at the start of EU regulation of medical devices in the early and mid-1990s under the device chief Mr. Bruce Burlington and David Kessler, the Commissioner of the FDA, and again as late as February 2011. Dr. Jeffrey Shuren, the current U.S. device chief, at the FDA in hearings organized by the House Energy and Commerce Committee’s Subcommittee on Health explained: “The FDA may take longer than the EU to approve some higher-risk devices because it asks for more robust clinical data to meet the “stronger US regulatory standards” (Sharma 03/19/2012).

In response to the question of whether the stricter US standards were resulting in safer devices, Representative Pitts is reported as having said: “But, according to recent studies, medical devices…[cleared by the] EU processes are statistically as safe as FDA-cleared or approved devices and have comparable outcomes.” Confirming the delays and practices of the FDA, AdvaMed states “with no discernible benefit in patient safety or outcome” (Sharma 03/19/2012). Maureen Kenny (2012), the chief editor of Script Regulatory Affairs, the leading regulatory journal in this sector worldwide, wrote on May 28, 2012: “US regulators have again chosen to defend their system of medical device regulation by denigrating the system in the EU.”

By way of summary, there is no scientific evidence to support the claim that the U.S. system is superior. An abundance of testimonies in congressional hearings makes clear that opinions among American scientists and business substantially diverge, as they do across the Atlantic (Maxwell 2012). In the absence of any objective criteria and measures, claims are easily staked behind concern that leadership may be slipping. What exists in the U.S. and the EU are different assumptions about law, medicine, and engineering, as well as very different political and regulatory processes, and different
ways of looking at devices and their risks and benefits. These are nurtured by highly variable but historically and culturally embedded normative legal, political, and economic influences, and unusual and different organizational, scientific and legal settings. Obviously, the claim about higher standards can more easily be made when it is backed up by power and reputation, not necessarily objective evidence. In sum, as long as the influence of regulatory science, the functioning of the advisory system, and the differences in the layers and layers of public and private law as between the US and the EU, including the integration of medical devices into the reimbursement scheme in national health programs in Europe, are not fully examined, the FDA’s claim about its use of more rigorous standards remains unsubstantiated. It is a fact that Congress and the FDA have defended and tolerated the status quo for 35 years; both in tandem have erred on the side of the principle of least burdensome regulation and faster access to the market. They drew a balance on the issues that really matter for patients - safety and effectiveness as well as benefits and risks – to the detriment of public health and patient safety. This time around the current debates may trigger legal changes and start a new era in device regulation.

The current level of criticism – based on empirical evidence rather than solely self-serving interests and ideology – is forcing the FDA-CDHR leadership to face up to the charges. In response, the FDA recommends improvements and offers updated guidance documents in a host of areas, including when and how to submit a 510(k) application (Newberger 2011; Sharma 12/21/2011). The FDA has been engaged in substantial efforts to rebalance its priorities, closely monitoring compliance and enforcement, including devoting more staff time and resources to post-market surveillance.

Prior to July 2011 when the FDA-commissioned report of the Institute of Medicine, an internationally respected scientific body, was published, and in response to growing domestic criticism of the slipping of the performance of the FDA since 2002, the FDA engaged in reviewing what changes might be necessary, doable, and not too controversial (FDA 2011b). In August 2010, it came out with 50 recommendations addressing medical devices in all three risk classes (I, II, and III). Twenty-five were chosen for immediate action, while the remaining more controversial elements needed to await the final report by the IOM. In early January 2011, the FDA announced that it planned to tackle three reform elements immediately (Eisenhart 2011):

(i) Streamlining the class III de novo classification process (in other words, addressing new high-risk devices submissions for market authorization),
(ii) “Clarifying the conditions under which 510(k) applicants must submit clinical data in order to make their review processes more efficient; and
(iii) Forming a Center Science Council made up of senior FDA experts to develop business processes and standard operating procedures (Eisenhart 2011).

One year later, developments are moving on. The FDA appears to be willing to “equalize” (Young 2012b) attention between pre-market and post-market activities in exchange for a deal with Congress: trading faster reviews for increased funding by Congress through the user fee program paid by the industry. The negotiations between
the FDA and the industry were tough and controversial. The FDA’s political strategy and tactics paid off.

The user fee program, which was up for renewal on September 30, 2012, for 2012-2017, was first established for a five-year period with the enactment of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA). It was reauthorized for another five years (2008-2012) under MDUFMA – the Food and Drug Administration Act of 2007. The bi-partisan votes in both houses on May 24, respectively May 31, 2012, and very little debate, are rare exceptional demonstrations of bi-partisanship in an otherwise dysfunctional Congress. This Congress is also interested in job creation and maintaining the industry’s international competitiveness. The amendment both covers and acknowledges the spectrum of past criticism ranging from the fast track 510(k) procedure, to stricter requirements for clinical studies, to conflicts of interest issues as well as better post-market surveillance. Accordingly, the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) would:

- “Allow the FDA more easily up-classify problematic devices so that subsequent, similar devices receive more scrutiny;
- Establish a timeframe for the FDA to finalize and implement regulations on unique device identification [to trace medical devices to patients];
- Add medical devices to the Sentinel initiative that was created five years ago as a mechanism to enhance post-market oversights of drugs;
- Codify the requirement that approval for high-risk devices in contingent on completing required post-market studies;
- Create a time line for so-called “522 post-market studies” for devices cleared by the fast track process; and
- Require the FDA to do more outreach to involve “non-conflicted” experts and groups in its recruitment efforts for medical device advisory committees” (Young 25 May, 2012)

The current user fee program (2007 – 2012) covers about 20% of the costs for reviewing medical devices in comparison to 60% for reviewing drugs. The Sunday Review (New York Times 04/28/2012) informs that according to a survey conducted by the Union of Concerned Scientists, 40% of the agency’s scientists felt that the consideration accorded to business interests was “too high”. As per the article, a report from the Public Citizen, a consumer advocacy group, “noted that device-related deaths had been running over 2,000 a year and the average number of high-risk and moderate-risk recalls had doubled in recent years." The FDA’s user fee program for 2013-2017 would provide new revenues ($595 million) as compared to the current ($287 million) allowing the hiring of 240 fulltime review process employees including 140 reviewers specifically for devices over five years (Pitts 2012). While the user fee program is perfectly legitimate and effective for some, it is causing deep concerns to others who view it as granting business undue influence over regulation and sidestepping the issue of who controls and influences whom, even if only 20% of the device budget is involved.

5 The New York Times published a correction on April 30, 2012, clarifying a mischaracterization of the survey. “Of 7,043 scientists sent the survey, 866 responded to a question on factors influencing FDA decisions and of those 40 percent felt that the consideration accorded to business interests was "too high."
Congress and lobbyists, who represent different segments of a highly heterogeneous med-tech industry, continue to argue in favor of fewer and softer regulation, faster approvals, and the continuation of FDA’s two-pronged approach to the market – through premarket notification (PMA) and the so-called 510(K) notification procedure – although they also concede a few areas that need improvement and/or tailor-made regulation depending on device-specific risks. Currently, a bi-partisan bill in the Senate, the Medical Device Regulatory Improvement Act (S1700), seeks to modernize the FDA’s review process. AdvaMed is reported as having been “especially encouraged to see the legislation’s focus on clarifying FDA data requirements, streamlining agency management processes and its emphasis on the importance of attracting the best experts to FDA advisory committees (Sharma 5/10/2011). In addition, a legislative package of ten bills was introduced in the House that all seek to “fix the FDA’s medical device regulation” (Sharma 5/10/2011). In tandem with Congress, the on-going debates in Congress and inside the FDA since 2010 all indicate that they intend to turn the FDA around and have it better serve in its role as protector of public health. A few years ago, the changes envisaged in this package were unthinkable. Change is coming but the question still remains: why did it not come earlier?

If the FDA had so much reputation and power in the past, why has it not used it to bring safe and performing medical implants and other devices on the market? Why has it asked the wrong questions about the safety and efficacy of stents and implants? The critics argue that it did not ask “the right questions” (Okie 2010, Maisel 2012; Voelker 2011; Zuckerman, Brown, and Nissen 2011). Indeed, even as late as 2009, when the FDA asked the IOM to review the 510(k) pre-market approval procedures for class II devices (moderate risk), the primary idea was hardly to ask whether a new medical device brings superior benefits to patients than existing, already approved and clinically used medical devices. For 35 years, the FDA has used “substantial equivalence” as a standard against which new applications were assessed, and it has accepted the industry’s claim that incremental changes are not changing the safety and effectiveness of devices which are “substantially equivalent” to an old device in use. Neither Congress nor the FDA considered changes.

7. Congress and the Medical Devices Amendment Act of 1976
Earlier we raised the issue of whether the FDA’s approach to device regulation is peculiar and unique and, second, what importance should be given to the historical origin of the 1976 Medical Devices legislation and its integration into an established organizational context, with the FDA serving as the center piece. In the language of the experts devices are either “preamendment or postamendment devices,” a term much in use which this paper will follow. It will quote to a great extent from the final IOM report and the two workshop reports and closely follow the language of the experts to avoid misrepresentation of complicated and subtle legal points (IOM 2011a).

The IOM found that the 1976 law “was designed in 1976 to provide only a determination of the substantial equivalence of a new device to an already marketed (predicate) device; it was not designed to determine whether a new device provides a
reasonable assurance of safety and effectiveness or whether it promotes innovation.” According to David R. Challoner, chair of the Committee on the Public Health Effectiveness of the FDA 510(k) Clearance Process. “[t]he committee struggled with how to address the conflict between the legislative framework of the program and the FDA’s stated goals” (IOM 2011a: xi-xii).

In retrospect, the Medical Device Amendment Acts of 1976 is a bizarre text that reveals much about legalese and congressional and FDA bureaucratic politics. All devices after 1976 were classified as Class III (high risk) devices; but specific exceptions were allowed (FFDCA § 513(f), 21 USC § 360c(f)(1) (2006)), which favored early commercialization and access to the market. Any medical devices that were considered “substantially equivalent” to a “type of device” defined as a device was classified as class II or class I device. For medical devices submitted to the FDA after 1976 a manufacturer could petition the FDA to classify the device as a class I and II device provided it could show that the new device was “substantially equivalent” to a pre-amendment device in class I or class II. The FDA was solely to be guided by considerations of risk when ruling on a petition. In reality, in line with the report of the IOM, the FDA faced an enormous task to process “increasing numbers of PMAs or have to go through a reclassification process that was procedurally cumbersome, labor-intensive, and time-consuming” (IOM 2011: 87). Instead, the FDA permitted the manufacturer of a postamendment device to demonstrate “substantial equivalence” to a preamendment device in Class I or II as part of the 510(k) submission” (87).

Where did the idea of “substantial equivalence” come from – Congress or the FDA? According to the IOM report, the FDA took a pragmatic and “liberal” interpretation. It cleared most postamendment devices in one of two ways: (i) as substantially equivalent to a preamendment device or “even to a postamendment device previously cleared through the 510(k) process (“a process known as piggybacking one device onto a series of precedents).” Fearing a legal challenge of its authority through a court-ruling, the FDA sought congressional ratification of its interpretation which it received in 1990. The new congressional text reads as follows:

“A. For purposes of determinations of substantial equivalence... the term "substantially equivalent" or "substantial equivalence" means, with respect to a device being compared to a predicate device, that the device has the same use as the predicate device and that [the FDA] by order has found that the device –

(i) has the same technological characteristics as the predicate device, or
(ii) has different technological characteristics and the information submitted that the device is substantially equivalent to the predicate device contains information, including clinical data if deemed necessary by [the FDA], that demonstrates that the device is as safe and effective as a legally marketed device and (II) does not raise different questions of safety and efficacy than the predicate device.

B. For purposes of subparagraph (A), the term "different technological characteristics" means, with respect to a device being compared to a predicate device, that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device” (IOM 2011a: 3 and 87).

One crucial point that the FDA cannot act, even if it wants to act, should be mentioned:
“Once a device is cleared through the 510(k) process and becomes eligible as a predicate, it cannot be removed from the pool of available predicates unless it has been banned or declared substantially adulterated or misbranded and pulled from the market” (IOM 2011a: 88).

Following two workshops, wide consultations, and debates inside the committee, it concluded that it would be preferable to design a medical device regulatory framework more in tune with the requirements of modern science, medicine and technology rather than keep an outdated 510(k) procedure. In the words of the chair of the committee, “the recommendations are focused not on making improvements in the 510(k) process but rather on steps needed to develop a more rational medical-device regulatory framework” (Challoner 2011:2).

Tellingly, in a highly unusual but orchestrated, tactical and defensive move in advance of the publication of the final report, AdvaMed (Advanced Medical Technology Association), the trade group that speaks for the US med-tech industry and majority of device companies, in a press release (dated July 29, 2011) attacked the IOM and its recommendation (AdvaMed 2011).

“The report’s conclusions do not deserve serious consideration from the Congress or the Administration. It proposes abandoning efforts to address the serious problems with the administration of the current program by replacing it at some unknown date with an untried, unproven and unspecified new legal structure. This would be a disservice to patients and the public health.

Numerous academic studies have shown that the 510(k) process is overwhelmingly safe (AdvaMed 2011).

It should be added that most studies were sponsored by device companies. By contrast, two regulatory experts argue (as do many authors) that “it would be shortsighted to forgo a thorough vetting on the strengths and weaknesses of IOM recommendations because the primary conclusion – that the 510(k) clearance process should be scrapped – seems too extreme to be realistically considered (Bailey and Kent 9/13/2011:1), ”Instead, the report should be carefully considered in the greater context of the ongoing reform process and dialogue between the FDA, industry, and the public to continue bringing improvements to the 510(k) programme” (Bailey and Kent 9/13/2011: 39). Some recommendations are “bold, yet vague,” and they have “merits and pitfalls” (Bailey and Kent 2011: 3).

In response to the seven recommendations for improving the 510(k) process and post-market surveillance capabilities that the CDRH had proposed, the chair of the IOM committee disagreed with CDHR in a letter to Dr. Shuren, the director of the CDHR: “As stated in its report, the IOM committee found that the FDA has a broad array of tools available to address safety concerns in the postmarket period but that the agency does not use these tools extensively. The FDA has not adequately explained the limitations of the tools and why it has not used them more widely. ... The IOM committee supports the concept of allowing conditional clearance based on postmarket surveillance in
appropriate cases and has suggested this option as a potential component of a modified de novo process” (Challoner 2011: 2).

Concluding comments
This first draft of a highly complex narrative pieced together the mosaic of device regulation from the most important features and striking observations about the regulation of medical device regulation by the US FDA. The draft did not go into details raising more questions that could be answered. Nor did we pursue interesting leads into a comprehensive cross-national comparison. While there are many aspects that fit Carpenter’s theory of reputation and power, the research at this stage does not warrant such final assessment.

There are strong calls for both close congressional oversight and substantial improvements and revisions of the 510(k) process by the FDA CDHR, improving the selection process of experts to the FDA’s advisory system, and limitations on conflict of interests. Given an abundance of bills before Congress and the upcoming presidential elections, we abstain from making any predictions of what the future regulatory framework for medical devices may look like in five years.

Building on literature on risk regulation and governance, analysts cannot ignore the fact that regulatory agencies are also embedded in different types of capitalism and political economies, with the Anglo-Saxon countries tending to be in one group and the continental countries in another. The political pressures in both the US and the EU on medical risk regulation are mounting and the FDA and the EU regulators face enormous challenges as technology becomes more complex and widely used. Indeed, a review of recent publications reveals a mixed picture, as does a review of the major regulatory components of medical device regulation in the United States. For every argument in defense of the FDA, available evidence suggests many counterarguments. To solve these riddles more research is needed.

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### Appendix 1 Differences between Pre-market Approval Applications and 510(k) Submissions (Statutory Framework as of July 29, 2011)

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Premarket Approval Application (PMA)</th>
<th>510(k) Submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed description of device component</td>
<td>Required</td>
<td>Not required</td>
</tr>
<tr>
<td>Detailed description of methods of manufacture</td>
<td>Required</td>
<td>Not required</td>
</tr>
<tr>
<td>Specimens of draft labeling</td>
<td>Required, reviewed, and approved</td>
<td>Required and reviewed, but not approved</td>
</tr>
<tr>
<td>Studies regarding safety and effectiveness</td>
<td>Reports of all studies relevant to safety and effectiveness required; clinical trials commonly required</td>
<td>Only studies demonstrating substantial equivalence to predicate needed; clinical infrequently needed</td>
</tr>
<tr>
<td>Filing fees (FY 2011) (regular business, small business)</td>
<td>$236,298; $59,075</td>
<td>$4,348; $2,174</td>
</tr>
<tr>
<td>Statutory time for FDA review</td>
<td>180 days</td>
<td>90 days</td>
</tr>
<tr>
<td>Conditions on final FDA action</td>
<td>Postapproval conditions authorized</td>
<td>Postclearance conditions not authorized</td>
</tr>
<tr>
<td>Need for FDA action on changes in manufacturing, labeling?</td>
<td>Generally, FDA approval required; thus, changes are subject to user fees</td>
<td>Generally, FDA clearance not required for manufacturing and labeling changes; thus, these changes are not subject to user fees; other changes – in design, materials, and intended uses – do require a new 510(k) submission.</td>
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