Global and Local Dynamics: The Regulation of Medical Technologies in The European Union, Japan and the United States

(Work in progress)

by

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Abstract

The regulation of medical technologies is a neglected topic in social science and health policy research and presents a real paradox given the increasing demands for life-enhancing medical devices, revolutionary medical-technological innovations, and the fact that recalls of medical implants, such as artificial hips, defibrillators, heart valves, and stents, are as frequent as drug recalls. In turn, global and national and in the case of the EU regional policymaking on medical devices has been shaped by three separate but mutually reinforcing developments: (1) the internationalization and globalization of medical device production, medical-technological innovation, and trade; (2) the imperatives of finding a single “window of regulation” driven by national regulators and global business interests; and (3) the persistence of strong regulatory preferences embedded in national institutional developments and legal and administrative traditions, including health care and medical research traditions.

This analysis starts out by exploring the commonalities of medical device regulation across three cases — the European Union, Japan, and the United States — and tracing their respective historical trajectories and examining how each regulatory regime is responding to, and is influenced by, global regulatory agreements designed to move toward a “single regulatory window” for medical products. Empirical data were obtained through interviews, websites of formal and informal stakeholders, and document analysis in each case. Preliminary findings suggest that the pressures for global cooperative agreements and their incorporation of global agreements into national practices and related adaptation processes are decisively influenced by the prevailing national institutional context, the commensurate political climate, and the historical-political trajectory unique to each case. In addition, patient access to advanced medical technologies is the least globalized component of medical device regulation and remains a function of each national health care system. Empirical data were obtained through interviews, websites of formal and informal stakeholders, and document analysis in each case.

Key words: Globalization; institutions, risk regulation; medical devices; European Union; Japan; United States of America; Global Harmonization Task Force; policy sector analysis.
Introduction
The regulation of medical devices is one of the most neglected topics in social science and health policy research. This is a paradox in light of the increasing demands for life-enhancing medical devices, revolutionary medical-technological innovations, and the fact that recalls of medical implants, such as artificial hips, defibrillators, heart valves, and stents, are as frequent as drug recalls.

How can regulatory policymaking and governance of medical technologies and related transformations of the regulatory regimes be studied in an empirical no-man’s land in Europe, Japan and the United States? While this paper starts with assembling the empirical elements, it is concerned with the following key questions: what are the primary regulatory issues and what are the factors that make them significant? What are the processes through which regulatory policy has evolved in the medical device sector and what are the factors which influence regulatory responses and the choice of policy instruments? What are the mechanisms for enforcement and implementation? And, finally, where do the pressures for global harmonization come from? From a problem-solving perspective, i.e. a patient perspective, the key issue is how to achieve and improve the quality, safety, efficacy/effectiveness of medical technologies while securing their performance during the entire life span of a device, even when already implanted in a patient.

The three regulatory frameworks have evolved in their own respective political economies, institutional settings, time periods, and social-political climates. Despite these differences, these regulatory regimes share similar objectives – listed in order of apparent priority – to ensure a level playing field for global trade, access to liberalized markets, and enhance human well-being and secure health protection. But the structures that support these objectives vary enormously and medical device sector regulation is a political domain with powerful opponents on both sides of the negotiating table: the medtech industry, trade associations and global device companies, as well as regulatory authorities and professional/industry experts who serve on advisory committees to provide the scientific input to the regulatory mission. These stakeholder groups form the “troika” of the “medical-industrial complex.”

A focus on medical device regulation alone (seen as product regulation) is insufficient for understanding the factors which influence regulatory responses, the choice of policy instruments and, most importantly, their enforcement and implementation. Enforcement and implementation of the full range of (i) regulatory policy heavily depend on (ii) the state-of-the-art clinical and medical research infrastructures and; (iii) the healthcare system where medical devices are used. These are the three interconnected conceptual and analytical components which set the overall framework for this work in progress.

This paper is a first attempt to provide a historical account of medical device regulation, the range and nature of regulatory issues on the agenda, and the recent changes in regulatory governance. This first attempt suffers from an unavoidable imbalance, with the U.S. case receiving more attention as the global leader in regulatory
responses, regulatory practices, and enforcement trends. The focus on the EU and EU member states and Japan will primarily focus on the recent institutional changes in regulatory governance specific to each country. A fine tuned analysis of each case will follow.

The comparison proceeds in several steps. It starts with a brief discussion why the study of medical device regulation and the three regulatory regimes can no longer be ignored as a topic for social science research. Next, the paper identifies and examines the commonalities these three cases share, while the fourth section focuses on the reimbursement of medical technologies by the payers of health care. By eliminating diagnostic products (IVDs) - hybrids between medical devices and drugs - we exclude a technological zone that reveals an even more complex regulatory environment than is the case with medical devices.

I. Why is the study of medical device regulation significant?

In theory, since thalidomide was discovered to cause birth defects in 1961, there has been a consensus in the international community that drugs, medical technologies and other products used in patient care must be subject to stricter regulation than other consumer goods. In practice, however, this consensus concerning regulatory affairs and the provision of medical care is compromised in varying degrees by the prevailing neoliberal Zeitgeist and a shifting balance of power among the major stakeholders. While regulators are struggling to keep up with the rapid pace of medical innovations, this softening of the consensus has been reinforced by the recent trend toward ever larger and interdependent markets on a global scale. These forces strongly influence recent developments and raise crucial questions of public policy briefly summarized below.

The first developments concern the rapid and revolutionary advances in several scientific disciplines and new applications of medicine and treatments, including their diffusion into the respective national health care system. Whether patients benefit from these medical innovations depends on the existing clinical infrastructures, clinical expertise, training and research resources, as well as the scientific input to the regulatory process, a process specific to each case.

Second, the imperative for global trade without borders and the strong push for early commercialization of new devices for new treatments by the industry require the building up new global institutions, like in other sectors in the global economy. Through the Global Harmonization Task Force (GHTF — a voluntary body of the medtech industry and the regulators of the advanced world — the national regulators and the medtech industry frame regulatory issues, set priorities, and choose the strategies of regulating medical devices for the 21st century. Despite modest efforts and its strong functional orientation covering a wide range of regulatory issues, the GHTF has failed to move beyond its preoccupation with the pre-market approval process and aggressively address patient safety issues (see figure 1).
Third, health care represents a personal and sensitive policy issue and the delivery of health care represents a highly localized or “least globalized” (Drezner 2007) element as a result of institutional restrictions. Numerous institutional constraints arise from three distinct local sources: (i) the trajectory of the medical device regulatory regime; (ii) the nature and evolution of the respective political-administrative system; and (iii) the inheritance of the particular ways health care is delivered, paid for and reimbursed in each case, including R&D in medicine. These are powerful forces that explain why healthcare remains a domestic issue in all three cases and why after-market clinical trials and patient safety issues will continue to be settled at the national level, and why the rhetoric about post-market surveillance transformation – advocated by FDA spokespersons – remains largely rhetoric. By the same token, rising public and private spending as a result of higher demands for advanced health care by an aging population, a change in disease patterns, and the continuous additions of new and sophisticated medical technologies are issues settled by national governments and payers who insist on cost and price controls over health spending and reimbursement. As a result, domestic governments and payers have kept reimbursement schemes covering the coding, coverage, reimbursement and technology assessment in health care (HTA) under tight national controls.

Reimbursement significantly impacts upon both R&D and clinical research though it is not the only source of funding R&D. The reimbursement processes, for example, in Germany, the United Kingdom and the United States as well as Japan are extremely heterogeneous and involve little transparency, with each country using different criteria for including or excluding devices from reimbursement. Further, payment may be denied by commercial or public insurers without explanation or recourse to evidence-based-medicine (EBM). In some cases, court rulings make the difference between a patient’s right to pay for life-prolonging drugs or medical procedure out-of-pocket without having their NHS/NHI treatment withdrawn (as has been the case until recently in the UK and Japan). In other cases, the criteria for accepting clinical data to prove the clinical efficacy of a medical device ex ante may have no bearing on the payers’ decisions on reimbursement ex post. And in the U.S., decisions by the Center for Medicare and Medicaid are not followed by the Veterans Administration, nor are decisions by CMS followed by commercial insurers. Additionally, reimbursement decisions by commercial insurers are not identical. These lacunae point to a lack of domestic policy coordination between the regulatory authorities, those who check on quality assurance and evidence-based medicine through technology assessment in health care, and those responsible for the delivery of health care.

Finally, the dependence of the FDA, the European Medicinal Evaluation Agency (EMEA) and national and Japanese quasi-independent regulatory agencies on intramural and extramural scientific advice brings to the fore potential conflicts of interest between device-maker and surgeons, device makers and purchasing agents (health facilities), and lobbyists and policymakers. The borderline between legitimate and illegitimate influences is fluid, and conflicts of interest issues only now begin to receive modest attention from both the media and the public. The alarming economic dependence of the regulatory agencies on user fees paid by the device makers to carry out their regulatory
responsibilities is unsettling and clearly answers the question: who controls the regulators?

II. Why is the study of these three regulatory regimes significant?

The political entities under review are two advanced industrial countries and the European Union as a regional block, consisting of 27 members. Politically, they are all democracies; economically, they are the leaders of the G7 and their industries are among the most productive and innovative in the world. They are among the founding members of the Global Harmonization Task Force (GHTF), created in 1993, and are supporters of global harmonization ensuring medical device safety, effectiveness and quality, international trade, and technological innovation. The GHTF’s five Study Groups (SGs) and the Steering Committee have since produced harmonized guidance documents laying out the international standards. Turning the SGs’ recommendations into reality has required political will, and this political will is present up to a certain point. International standards and guidance documents may, but need not, be applied in domestic implementation.

The global agenda items about which global players seek political consensus are (i) premarket approval and harmonized product labeling requirements; (ii) adverse event reporting; (iii) post-market surveillance; (iv) quality systems requirements; (v) regulatory auditing of quality management systems; and (vi) evidence of clinical safety (clinical data). These developments taken together affect patients around the globe, who are the ultimate beneficiaries or victims of medical technologies.

The healthcare systems of all three regulatory regimes – the least globalized and most decentralized elements – provide medicine of the highest quality, although each case significantly differs in the structural foundations, orientations, and goals. For example, the medical device sector represents about fifteen per cent in the U.S. and about seven to eight per cent of healthcare spending in both the EU member states and Japan (Table 1). The healthcare systems use public and private financing and avail themselves of public, private and for profit organizations for delivering health services. In addition, these systems share similar methods for coverage, reimbursement, and compensation schemes, which are at the heart of recent health care reform. In addition, these systems constitute the most important methods and mechanisms, which in turn determine patient access to medical technologies. Their respective populations enjoy the highest living standards but their epidemiological profile defies easy conclusions indicating resources and knowledge or the amount of public or private spending on medical technology and health care are positively correlated.

[Table 1 Medical Device Highlights for the U.S., EU, and Japan]

Significant developments in the medical device sector have taken place over the last decade that merit attention. On the supply side, globalization has opened up new markets in Asia, Latin America and Central, and Eastern Europe, but less in Africa. At the same time, the number of device makers and suppliers has increased enormously.
These include the 20 to 30 global companies which run global operations, however, many of these small and medium-sized start-ups look for new markets abroad to sell their products, outsource their manufacture, and sometimes promote clinical trials and studies. As a result, lack of familiarity with foreign health care systems adds complexity to an already intricate regulatory regime.

Trade with medical devices (about 8,000 different types are marketed on the world market) is a $180 billion business a year and growing at a steady pace. The U.S.-led medical device industry greatly outpaces the foreign competitors in terms of sales, trade volume, innovations, competitiveness (understood as R&D, patents, and publications), and along many other dimensions (Hanson in Burns 2005). Seventeen top global U.S. companies (out of a total of 20 global traders) supply most of the sophisticated advanced medical technologies in the U.S., the European Union, Japan and other parts of the world. Only three European companies – Siemens Medical Solutions, Philips Medical Systems and Becton Dickinson & Co. – make the cut. The only Japanese company in this league is Terumo, which ranks 25th on the world list.

Despite the current neo-liberal language of deregulation and liberalization of markets, unlimited access to the U.S., EU and the Japanese medical device markets is not secured anywhere. In none of the three cases is medical device regulation solely self-regulated by the medical industry. While numerous legal mandates apply to the medical device sector, *grosso modo* they tend to favor their respective medical device communities. In light of this situation, many devices have only recently been subject to regulation or remain completely unregulated.

According to the U.S.-led industry, trade with medical devices is seriously hampered by four serious impediments: (i) inadequate reimbursements of devices by Medicare and commercial insurers in the U.S., and by publicly sponsored and regulated health care systems in the EU and Japan; (ii) the price controls payers impose; (iii) the sole funding of R&D by the U.S. med-tech industry and the so-called “free riding” patients around the globe, and, finally; (iv) the slow, cumbersome and intransparent regulatory processes abroad. It comes as no surprise then that the med-tech lobby led by the U.S.-based Advanced Medical Technology Association (AdvaMed, previously HIMA until 2000) and individual device companies are present whenever and wherever opportunities to promote their cause and economic interests exist. AdvaMed makes its voice loudly heard in the corridors of political institutions in the U.S. and in high level negotiations within the European Union and Japan.

In early 2008, Mr. Stephen Ubl, president of AdvaMed, asked the U.S. Congress to assist the administration “…to actively oppose excessive regulation, government price controls, foreign reference pricing schemes, and arbitrary across-the-board reimbursement cuts imposed on foreign medical devices and diagnostics” (RAJ Devices 2008: 48). AdvaMed’s strategic political involvement at the highest governmental levels will have strong implications for future bi-lateral and multilateral trade negotiations between the U.S., the EU, and Japan and other countries as well. While this battle cry will resonate in trade relations, it should be stressed that regulation, price controls,
reference pricing, and balanced reimbursement are the very elements that provide the glue for affordable, equitable, and solidarity-based universal health care in Japan and the EU member states. Who is going to prevail over whom is central to this research.

Predictably, the industry has in store two solutions. Concerning reimbursement by the payers of the healthcare system, countries should adopt: (i) clear and transparent decision-making rules – concerning coding, reimbursing, pricing, etc.; (ii) reasonable time frames for decision-making; (iii) data requirements sensitive to the medical innovative process; (iv) reimbursement rates based on conditions in each country; (v) allowing technology companies to participate in decision-making; and (vi) a meaningful appeals process (RAJ Devices 2008: 48). Regarding appropriate regulatory responses, AdvaMed believes that the most significant tools to implement medical device regulatory policy in a world without borders should be: (i) acceptance of non-binding international standards; (ii) transparency and national treatment; (iii) harmonized inspection practice; (iv) mutual recognition of product approvals (or at least of the data used for them); (v) harmonized auditing and vigilance reporting rules; and (vi) use of independent accredited bodies for inspection and approvals. These issues constitute the central themes around which this comparison is organized.

To expedite the approval processes and global harmonization, transnational and international expert communities of clinicians, scientists and industry experts provide the quality and scientific input to regulatory policymaking by seeking a consensus on appropriate clinical standards, clinical evaluations, best practices, patient registries, etc. Unfortunately, despite the project’s promises and flowery language, early and expedited approval processes without the necessary clinical tests, real time data, and experience of surgeons with the safety and effectiveness of new devices have serious downsides, above all, for patients.

The controversies surrounding R&D funding and “free riding” patients exceed this paper’s objectives. In general, device makers operating on a global scale are known to be able to afford the cost of R&D, while small and medium-sized device companies are rarely involved in R&D. There is also public funding for biomedical research, which commercial venture capitalists will exploit when promising results are on the horizon. As long as these basic research activities are not included, the information on R&D funding provided by the industry is both incomplete and misleading. For example, in the U.S., device makers, notably the cardiac sector, have benefited from funded research through NIH and NASA. A March 2007 report of the U.S. International Trade Commission mentions (U.S. ITC 2007, ch.3: 1-3) cardiac defibrillators, magnetic resonance equipment, and nuclear imaging devices as having benefited from NIH funding. Another relatively new source of funding of basic research is the National Institute of Imaging and Bioengineering (NIBIB). Created by Congress in 2000, the NIBIB is the newest NIH institute (U.S. ITC 2007: 11-12). Basic and applied research has also been funded by the National Aeronautics and Space Administration (NASA), which made NIH bioengineering grants for applied research related to medical technology in the amount of $1.3 billion in 2005. Beneficiaries were U.S. firms such as Spacelabs, Hewlett-Packard, and Marquette Electronics.
In all three political entities, there are pro-globalization advocates and free traders who promote measures designed to facilitate trade, level the playing field, and lift existing non-tariff hurdles. Such non-tariff obstacles include constraining reimbursement schemes and prohibitions on direct-consumer-advertisement of medical devices (except in the U.S), and limiting the many legal and linguistic hurdles encountered in regulation. Despite these obstacles, policymakers, experts, and opinion leaders in scientific medicine share a consensus that the objective of regulation is regulating medical devices for trade and the protection of patients from unsafe, low quality, and inefficacious/ineffective products. This consensus leaves considerable room for assessment and interpretation.

Case selection is justified by the available data on the world market and the industry. When data are broken down by markets, the U.S. is the largest market (50%), followed by the European Union (30%), Japan (10%), and others (10%). If the data are broken down by traders, the EU is leading (30%) followed by the U.S. (29%), Japan (9%), China (4%) and Switzerland (4%) (U.S. ITC 2007, ch.1: 3-4). By all indicators, the industry is a growth industry, with the U.S.-led med-tech industry registering a growth rate of 7% or 8% per year. Depending on the market and the product type, the growth rate varies from a low of 8% up to 15% – 20%. Consequently, yet another crucial issue is how to reconcile the pressures for increasingly larger markets with the need for maintaining and strengthening public health and health protection for real people living at the grass roots.

As mentioned previously, the demand for life-extending and life-supporting devices is increasing due to aging populations everywhere. As of 2003, Japan ranks first in the world with 20% of the population over the age of 65, followed by 17% on average in the European Union, and about 12% in the U.S. (U.S. ITC 2007: xiv). Qualitatively, the regulation of medical devices has always required a balancing act between competing objectives – trade, the commercialization of medical innovations, and profits, on the one hand, and patient safety on the other. In other words, to strike a balance between the promotion of medical technologies and the protection of patients from their use has always been necessary. For patient safety the balancing act involves a double-edged sword of granting early access to new and promising devices while simultaneously securing appropriate guarantees on safety and quality. Finding the right balance between early release and medical device safety and effectiveness has become more complex in the last five years, as more sophisticated and complicated devices – summarily referred to as advanced therapies - are introduced to the market at an ever increasing speed.

The single most important influential factor on medical device regulation needs to be stressed again. The medical technology expertise and knowledge are in the hands of the device makers, with the regulatory authorities often seriously lagging behind in terms of overall knowledge largely because they suffer from manpower shortages and lack scientific expertise. This imbalance, brought about by the dramatic advances in technologies, materials engineering and computer-driven technologies, presents serious challenges to the regulators to act objectively and make decisions on the basis of regulatory science and their own analyses rather than on the basis of politics and political
pressures to minimize the role of regulation. Still, whatever the regulatory disagreements, regulators and industry and other vested economic interests alike all claim to share the same goals: swift market access, legal certainty, and patient protection.

Finally, the manner in which these three political entities and the dominant stakeholders bring regulatory science and their influence and power to bear on medical device regulation counts in the international system. All three cases are deeply implicated in the larger processes of globalization and the internationalization of regulatory affairs, which lead to three core arguments of this paper. First, medical device regulation, regardless of the level where it occurs and how it has evolved, has as much impact on the market behavior and strategies of device companies as it has on patients’ early or late access to effective and advanced medical technologies. Second, the pressures for global cooperative agreements come from new technologies, a globally operating industry, and locally delivered health care. How these three universes interact with each other substantially depends on the institutionalization of a first template of medical device regulation and its subsequent transformations in the U.S., EU, and Japan. Third, the global and national regulatory responses to new technologies (e.g., combination products, diagnostic-related products (IVDs), cell and tissue engineered products, etc.) very much depend on the nature of the new technologies, which can, but need not, include tailor-made and product-specific regulatory responses. Global regulatory efforts are expected to bring higher safety and patient thresholds than national regulation but even if true these efforts will not improve patient access to new medical technologies. Much depends on how the demand for innovation and added value of medical technologies in clinical care will be reconciled with expanding patient access to medical technologies in a climate of cost containment policies that are rigorously pursued by the EU member states, Japan and the U.S.

II Varieties of literature linking international and national regulatory policymaking on medical technologies

There is no single set of literature that helps explain the observed variations across the U.S., EU, and Japanese regulatory regimes. Nor is there a literature that can explain why device-makers and regulatory authorities cooperate at the global level or which regime’s regulatory approach will become the new global model. The public policy literature explaining policy change (Sabatier 1999, 2006; Birkland 2004, Kingdon 1995; Baumgarten and Jones 1993) is limited for cross-national research, as the empirical evidence is drawn exclusively from a fairly unique historical-political experience in the U.S. The recent writings on comparative political systems, politics, democratization, public administration and the new public management (NPM) are helpful, but they do not adequately account for the overall pattern of regulatory policymaking and the role of business and regulators in a domestic, regional or international contexts.

Policy sector analysis and historical-institutional analysis are the most promising analytical perspectives for this comparative work. Without going into a detailed discussion of historical-institutionalism, the domestic foundation of medical device implementation structures and sectoral governance with a focus on the “differentiating factors and causal mechanisms” unique to the medical device sector (Scharpf 1999) can
safely be argued to be rooted in the national context in each case. The political economy, the prevailing legal, administrative, and professional, as well as state-industry traditions, offer many of the answers concerning where the ideas (not necessarily remedies) for regulatory agreements at the global level originate and, in turn, how they may or may not be adapted to national practices. In turn, scholarship on the international political economy (Castles 1989: 1-15; Hall and Skopce 2004; Davos and Braitwaite 1998, Braithwater 2008) offers useful insights for explaining the emerging global configurations in this sector, such as the Global Harmonization Task Force with its five study groups (SGs), ad hoc working groups representing the troika of the medical device industry, as well as the transnational expert communities which provide the scientific input to risk regulation and policy making.

Additional insights can be gained from recent comparative health policy scholarship with a focus on policy transfer and the ability of policymakers to learn and draw appropriate lessons from the policymaking experiences in other countries (Marmor, Freeman and Okma 2005). However, this literature stops short of providing clues about risks and risk regulation, which is at the heart of medical device regulation, and usually excludes a focus on implementation. But implementation is key to any policy and vital for any assessment of policy outcomes. With the exception of scholarship on medical technologies in the history of medicine and sociology (Timmermann and Anderson 2006) and technology in health care (Cohen and Hanf 2007), a social science literature on the medical device sector hardly exist.

Recent literature on regulation has produced several explanations of the general evolution of regulatory regimes in the last two decades (Jordana and Lévi-Faur 2005; Chayes and Chayes 1995; Braithwaite 2008; Braithwaite and Drahos 2000). The first and most challenging topic is the search for global regulatory governance and the ability to promote its political authority and legitimacy in a rapidly changing, borderless world (Grande and Pauly 2005; Héritier 2002). Because of its proximity to the med-tech industry and in regard to its design, the work closest to this research on medical devices is the comparative research on the pharmaceutical biotechnology industry in the U.S., Germany, and Switzerland by Robert Kaiser. It can be argued that in the United States, as in the case of the pharmaceutical industry, a similar constellation of deep seated structural differences together with the availability of venture capital for start-ups may explain the advantages attributed to the U.S. medical device industry. Finally, Daniel Drezner (2007) convincingly argues that “[d]espite globalization, states – especially the great powers still dominate international regulatory regimes, and the regulatory goals of states are driven by their domestic interests.” Drezner adds:

“The great powers – the U.S. and the EU – remain the key players in writing global regulations, and their power is due to the size of their internal economic markets. If they agree, there will be effective global governance. If they don’t agree, governance will be fragmented or ineffective. And, paradoxically, the most powerful sources of great-power preferences are the least globalized elements of their economies.”
His empirical illustrations are taken from a variety of sectors. Internet, finance, genetically modified organisms, and intellectual property rights. Yet the similarities with the dominant role of the U.S. FDA and the EU in the medical device sector and in the Global Harmonization Task Force are striking. The two prototypes of medical device regulation that are of any relevance in the international arena are the US and the EU regulatory models. The European model of compliance rests on standards as the basis for establishing and assessing safety and performance and the US model of comparison with similar devices that already exist and are deemed satisfactory as a basis for setting and measuring safety and effectiveness. These differences are not insignificant; they reflect broader philosophical, historical and material differences.

The logics behind regulation – normative, political, economic as well as scientific – differ fundamentally along a number of dimensions: state-business relations in the political economy, the power balance between government/regulator or, in the case of the EU, third party certification bodies and firms specific to the medical device sector, as well as the embedded mechanisms of channeling scientific knowledge into the decisionmaking process on risk regulation of medical devices. As Michelle Egan (2001:26-27) summarized the key differences, “[T]he US preference is for standards set by the market after competition between different technologies, and the European preference is for standards created through institutionalized industry cooperation” or through an “industrial policy.”

Historical-institutional theory predicts that these root differences will most likely represent the key factors explaining how transnational regulatory convergence, including the likely adaptation of global agreements into on-going national regulatory processes and, ultimately, clinical practice in medical device-specific cases. An institutionalist perspective also predicts that these differences will continue to count for a renewed problem definition, the formulation of regulatory responses and implementation processes, all of which take place nationally.

Drezner’s analysis also offers good reasons why an explanation of regulatory regimes in the field of medical devices may benefit from broader explanations of institutional developments in each country. Important topics include the preferences of the stakeholders, structural power relationships embedded within the political economy, the internal differentiation of the med-tech business world, the complexity of the medical device manufacturing environment, and the emerging new forms of global governance. One main interest of this paper is to show how risk-based medical device regulation counts in global debates through “uploading,” and how global agreements are incorporated into national practices through “downloading” in simultaneous two-way bottom-up and top-down processes.

III. Commonalities of Shared Macro Risk Regulatory Policy
Despite global harmonization, preliminary research concludes that the regulatory regimes for medical devices in the U.S., EU and Japan continue to differ widely while converging at the same time. All three regimes are part of a re-regulation movement but have also relied on a good deal of self-regulation, co-regulation in the case of the European Union
and its 27 member states\textsuperscript{10} or no regulation.\textsuperscript{11} The global developments are driven by three forces: the economic interests of globally operating device manufacturers, the interests of patients for globally agreed upon universal safeguards in a world of trade without borders, and the transformative nature of new technologies. A less obvious item driving the dynamics of the strategies and tactics of the negotiating parties at the global level concerns whose approach to regulating medical devices should serve as prototype, and which model will and can reconcile the competing objectives of trade-oriented or patient safety-oriented regulating while keeping transaction costs to a minimum? Field interviews suggest that the willingness to agree to global harmonization very much depends on whether global harmonization requires new domestic legislation. This issue is pertinent in all three cases and will be fully explored later. The following section will examine the commonalities of the three regimes.

\textbf{Difference in timing.}

The most obvious comparative observation is the difference in timing of the three regimes. The U.S. took an early lead, starting at the turn of the 20\textsuperscript{th} century, but seriously focusing on regulation in the mid 1970s, while the EU and Japan regulatory regimes responded to the pressures of globalization and the internationalization of regulatory affair in the early 1990s. Despite this difference in timing, they share similar legislative and institutional developments. Regardless of all three medical device regimes’ foundations, subsequent legislation and institutional developments were directly influenced by their development, with the fledgling medical device framework in each case generating multiple effects: setting the speed of institutional transformation, determining the kind of regulatory adjustments, and framing the arguments for global regulatory solutions, all of which are rooted in national practices or borrowed through ‘benchmarking’ and ‘best practice.’

\textbf{Evolution from within drug regulation.}

In all three cases, medical device regulation in varying degrees evolved from within drug regulation before splitting off from it and turning into a legally autonomous medical device regulatory framework. The timing of this process of moving away from the drug regime occurred at different periods – in the U.S. in 1976, the EU in 1990. In contrast, in Japan, the 2005 PAL continues to serve as overarching framework for medical devices. This separation process was brought about by enormous, if not dramatic, product innovations and internal product differentiation – for example, medical device vs IVDs vs. stem cells vs. blood products, high-tech equipment vs. life-assisting consumer goods at home, etc.. This product differentiation is due to progress in materials engineering, nanotechnology, and computer-driven as well as e-driven innovations over the last decade – known among technology experts as “the sectoral adaptive capacity of new technologies” (Dolata 2007).\textsuperscript{12} The issues remain the same. How to regulate new high-risk devices in the highest risk category class III and notably advanced therapies (e.g. gene therapy, cell therapy and tissue engineering)? Because these new technologies increasingly blur the borderlines between drugs and medical devices, should the regulation remain under the drug framework, be close to but not integrated with the respective drug regime, or, institutionalized under the medical device regime?
The ‘life cycle’ concept.
A third experience common to all three is the endorsement of the “life cycle concept.” Regardless of the CDHR’s simple “life cycle” concept or the more recent encompassing “total product life cycle” concept,13 both versions are the backbone of the risk regulation framework. The concept stands for the various stages of the regulatory process and clearly stipulates the responsibilities of the dominant stakeholders at a particular stage: device makers, vendors/distributors and users. The “life cycle concept” covers pre-market approvals, including the submission of clinical evidence ex ante and post-market surveillance and medical vigilance responsibilities, including after market clinical studies ex post. The “life cycle concept” also stands for extraordinarily complex processes which are unique to this sector and make generalizing for the entire sector difficult if not impossible. A risk to a patient may be product-specific and also dependent on which procedure is used.

Following the OECD’s broader understanding of regulatory management (1997), risk management (rather than risk assessment and evaluation both requiring scientific professional expertise) is no longer limited to device makers alone but is a shared responsibility of (i) manufacturers, (ii) the health care system and (iii) public health authorities. Empirically, the institutional linkages among the stakeholders vary widely across the three cases, as do the compliance and accountability mechanisms. In the past, all regulators devoted much of their time to the pre-market approval process in all three regimes, but their attention is claimed to be shifting to the post-market stage and the three clusters of postmarket problems, as outlined in figure 1.

[Figure 1: CDHR PMS Transformation Connecting the Dots]

No space for patient voices.
Neither the EU medical device regime, nor regulatory governance in the U.S. and Japan grants patients a distinctive voice in any of the regulatory stages of the “life cycle concept.” Nor does the work of the GHTF and its various study groups and transnational expert committees foresee a space for patient voices. To the extent that patient rights are institutionalized, they are woven into layers of complex national rules, procedures, and practices, which tend to be external to medical device regulation but are instead embedded in the regulatory space governing the delivery of healthcare and the conduct of clinical trials and research.

Risk-based regulation and policymaking.
Risk regulation is a fifth common feature based on a three or four part classification scheme in the U.S., EU and Japan. In the highest and lowest risk categories, there are relatively few and small differences, yet in class IIa/b (EU) the differences can be substantial, as in the category of “existing or known medical devices” or in the definition of “intended use” (Laufer 1998: 112). The same can be said about what constitutes “new medical devices” under FDA regulation.
In the U.S., devices fall into three categories – I, II, or III, with class III devices with the highest risks and hence requiring the most stringent controls. Rather than copying the U.S. classification, the EU introduced a four-class scheme. Devices fall into class I, IIa, IIb, and III. Rather than a public authority, certification bodies (or notified bodies) implement and monitor compliance with EU rules, with varying involvement of a competent authority depending on the risk category of a medical product. None of the classification system is written in stone. For example, in 2004 key products in the implant sector (knee, shoulder, hip, heart, skin, breast) were reclassified from IIb to III, the highest risk category, in EU law in 2004, with significant variations in implementation by the EU member states. Although facing much opposition, in the U.S., the FDA is pursuing reclassifications downward from the highest-risk category Class III to medium-risk class II category (http://www.medicaldevicestoday.com/2008/06/cdrh-chief-push.html.). In Japan, the revision of its classification system in 2005 combines both EU and FDA practices. Class I can be put on the market without any intermediary. Class II require a third party certification after 2005. Class III and Class IV need government approval, which comes in two steps. The PMDA, a regulatory agency created in 2004, reviews, evaluates and recommends decisions to the Ministry of Health, Labor and Welfare (MHLW), but it has no authority to make final decisions. MHLW is a strong central ministry combining political authority and responsibility for the entire medical device regulatory framework, the national health protection system (NHI), public health, as well as medical facilities, in addition to the many competences over labor and welfare issues.

**Innovation and conflicts of interest.**

The recent decision by the FDA to bring more transparency to innovative processes highlights another side of risk regulation, raising complex issues for all three regimes. Simply stated, “transformative sectoral capacities of new technologies” (Dolata 2007) can hardly exist without close device maker-surgeon relations. Typically, medical advances are initiated by the industry and perfected by practicing surgeons, but sometimes device makers approach surgeons to work with them. Additionally, surgeons sometimes come up with ideas for a new design and approach. Because clinical investigators/ surgeons wear several hats and conflicts of interest are abundant, they should not be put under the rug. They serve in (i) advisory roles as product sponsors in various market approval processes *a priori* and monitoring processes *a posteriori*; (ii) use advanced technology when they diagnose and treat patients; and ultimately they (iii) carry out and assess the validity of after market clinical studies. Clinical investigators may engage in practices harmful to patients. For example, as sponsor-investigator, they may enroll patients in device clinical trials before the regulator gives approval of a device clinical trial or they may enroll more patients than approved. They may fail to obtain proper informed consent or schedule follow-up visits, and commit other improper actions. Research concludes that sponsors-investigators, even renowned surgeons in a specialty, often have limited training in the conduct of clinical trials (Barnett Educational Services 2005).

Turning to the device makers, leading global companies are known to occasionally engage in questionable, if unacceptable and unethical activities by
withholding the results of clinical trials (positive and negative) and not sharing them with surgeons who continue to use them (despite the known risk of premature malfunctioning), encouraging the off-label use of medical devices, and supporting direct consumer-advertisements, including consumer-oriented assisting devices such as implants. It should be noted that DCAs are prohibited in practically all advanced countries except the United States.

In the FDA Amendments Act of 2007 Congress gave the FDA stronger authorities in response to the revelations mentioned above. At first, the FDA did not take advantage of their increased authority, but by early 2008 both AdvaMed and the FDA have responded with stricter measures and guidelines. Draft legislation supported by AdvaMed that is before Congress would require device makers to reveal all payments to and consultancy arrangements with orthopedic surgeons. Under the heading Fraud and Abuse: Walking the Compliance Line. The Do’s and Don’ts of Device Marketing, AdvaMed offers training for compliance officers, in-house counsels, sales and marketing executives and senior management. The ad states:

“As government regulation and scrutiny of medical technology companies increases, so too does the risk of non-compliance and exposure to severe civil and criminal penalties.

Now more than ever, companies must be certain that sales and marketing practices do not violate what is permitted by law. So how do you navigate the fine line between practices that create star performers in other industries and felons in this one?

A challenge? Yes. But, the risks of remaining uninformed are too great compared to the cost of learning how to avoid them.

...this program uses didactic sessions and role-playing examples to convey with alarming clarity the risks and consequences medical technology companies may face and the protocols necessary to prevent them.”

In sum, the stakeholders acknowledge the seriousness of the problems which need repair and they recognize that they need to strike a better balance between an aggressive push for sales/marketing and the protection of patients.

**Delegation to Independent Regulatory Agencies.**

Of all recent public-sector developments since the 1990s, the phenomenon of delegating regulatory authority to independent agencies is found across highly diverse policy sectors and experienced by countries at different levels of development (Lévi-Faur 2008). Theoretically, the delegation of regulatory powers to independent agencies is a byproduct of the current neoliberal Zeitgeist: privatization and market liberalization over the last two decades. Empirically, the delegation of regulatory powers in the field of medical technologies comes in different forms and structures, with the spectrum ranging from the FDA’s Center for Devices and Radiological Health (CDHR) to the new and varied forms found in EU member states starting in the early 1990s and in Japan with PMDA in 2004. What the FDA does, how it views the universe of medical devices, and how it sets enforcement trends is of key interest to the industry and regulators from all corners of the globe.
(i) Medical device risk regulation in the shadow of the drug regime. The field research suggests two observations are applicable to all agencies regardless of status, size, experience and longevity. First and foremost, due to the priority given to medicinal regulation, medical device regulatory regimes — located inside the agencies — remain hidden in the shadows of drug regimes. Second, their establishment is invariably the result of the economic and political pressures for global solutions driven by globally operating device makers and those regulators from around the world who share the same interests. The industry seeks legal transparency, speed to market for their medical products, and access to new markets while patients and the general public may want political transparency and fully tested efficacious products. The organizational separation of regulatory functions from health care service functions inside a ministry of health through their transfer to “independent” regulatory agencies is a by-product of the same pressures. Despite their different legal and organizational status, the agencies in the three cases share similar configurations.

(ii) Dependence on user fees. In the U.S., EU member states and Japan, user fees are the primary source of funding for the approval processes by regulatory agencies. This dependence on user fees has an upside and a downside. Theoretically and normatively, user fees are legitimized by an ever increasing tendency to privatize regulatory policymaking; empirically, lawmakers who legitimize user fees to carry out regulatory functions argue that the current budget constraints leave no other choice. However, this near and alarming dependence on user fees and the knowledge of the device makers could potentially lead to a loss of trust, professionalism, and integrity. In the U.S. alone, medical supply companies spent more than $28 million on lobbying during 2007. In the cardiac sector, three top global operators – Medtronic, Boston Scientific and St. Jude Medical – are among the most generous and demanding for their interests. Medtronic spent $1.7 million lobbying the federal government, its rival Boston Scientific $1.96 million, and St. Jude Medical a negligible sum of $460,000! (Snowbeck 2008; McElhatton 2008). This level of activity and donation is closely associated with draft legislation before Congress: Medicare and user fees for the FDA. In the United States, Democrats and Republicans benefit equally (Clinica # 1299, 2008: 11). Very little is known about donations to political campaigns and sales practices in other countries.

(iii) Up-to-date in-house and top-notch scientific expertise. Are independent regulatory agencies adequately prepared to protect patients? Looking at the U.S. alone, the Institute of Medicine, the Government Accountability Office and the FDA’s own Science Board (New York Times 2008: 13) issued alarming reports on the “poor management” and “scientific inadequacies” regarding the FDA’s ability to protect the country against unsafe drugs, medical devices and food (RAJ Devices 2008:9-12). Commenting on a few of the problems found within the FDA, Dr. Gail Cassell, chair of the Science Board’s Science and Technology Subcommittee (and simultaneously vice
president of scientific affairs at drugs company Eli Lilly) made the following observations:

1. “The FDA’s evaluation methods have not kept pace with major advances in medical devices and use of products in combination.”
2. “The pace of scientific discovery and complexity of new products have left the agency struggling with increased workload and a chronic shortage of funds.”
3. “The FDA has no systems to store data from clinical trials or adverse event reporting.”
4. “The FDA has been forced into a position of fire-fighting instead of pursuing a proactive culture of regulatory science.”

An alleged shift to post-marketing problems – observable across all three cases but not working at a satisfactory level - is prompted by a structural dilemma inherent in medical devices. Not all risks are detectable in ex ante evaluations and are gained only with experience of the use of devices with a larger patient population. Hence the FDA and invariably European and Japanese regulators distinguish between adverse events related to medical device use as distinct from those related to a medical device as a product. For its part, the FDA’s Center for Devices and Radiological Health (CDHR) focuses on “new, high risk, and complex devices” (CDHR 2006) and operates a complex system of monitoring and responding to adverse events and risks associated with the use of medical devices available on the market, but it is not adequate. The FDA admits that the CDHR is inadequate, acknowledging that in the U.S. “as few as 1 in 100 medical device events are actually reported” (CDHR 2006: 5). Knowledge about the cause of adverse events is extremely limited in all three cases, and important data are missing, and even if they were available, they would hardly be comparable across regulatory systems.

(iv) Extramural advisory committees and scientific advice. The regulatory agencies in the three cases use outside experts to serve on all kinds of advisory committees at home, in EU transnational and international expert communities (such as the GHTF’s working groups and study groups), and in the international and regional standard setting committees, such as ISO/IEC. Clinical investigators play a critical part in the approval process of medical devices ex ante and an even more important role in post-market surveillance and clinical studies in the U.S., the EU member states and Japan. In FDA’s case, after market clinical studies are mandated as a condition for approval of medical devices in about half of all applications for market approval by the FDA-CDRH. This raises the question of whether communication channels and organizational links between the regulatory track and the service delivery track are in place. If the appropriate channels and links are in place, are they working in a coordinated or compartmentalized fashion?

In the last two years, practices by medical device companies have come to light which are viewed as improper and unethical by some and unavoidable by others. The impartiality of scientific advice giving and standard practices in the industry to reward scientists through special consultancy arrangements, kickbacks, bribes, paid vacations, etc., are fundamentally challenged. Contacts between device makers and surgeons by definition are close. Surgeons play crucial roles before, during, and after surgery. The surgeon recommends a particular procedure, implants it, and supervises the patient in post-surgery recovery. This raises the questions about where to draw the line between
IV. Introducing the second pillar of access to medical technologies: Coding, Coverage, and Reimbursement

External and co-evolving to the medical device regime, which has been the focus so far, is a second pillar that influences both medical device regulation and patient access to medical technologies. This pillar involves national healthcare systems and their respective complex governance, funding and delivery systems. How decision making has been organized historically, politically, organizationally as well procedurally has substantial implications for patient access to medical technologies. Short of unraveling complex details – misleadingly perceived as too technical to be of interest to social scientists – there is no way of knowing how health care reform and access to medical technologies interact with each other and affect the outcome, that is, access to medical treatment. Funding and reimbursement are also perfect examples that show how global forces impact upon the most localized processes in health care in significant ways, and how these localized processes may privilege the regulatory status quo over a new globally more binding regulatory model (like the ICH – the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Reimbursement, coding issues, and processes are the most localized and least globalized aspect of regulating medical technologies in all three cases. Even in the European Union where medical device regulation is more or less uniform EU-wide, the funding and reimbursement remains a national power.

Most scholars who study health protection schemes in different countries cross-nationally have wrestled with understanding the causes and effects of national health care reform on spending, access, quality of care, organizational changes, etc. (Campbell and Ikegamia 1998; Ikegamia and Campbell 2008; Ikegami and Campbell 2004, Ikegami 2007; EU Saltman, Busse and Figueras 2004; Saltman, Figuers and Sakellarides 1998; Esping Anderson 1990; Mossialos and McKee 2002; McKee, Mossialos and Baetens 2002; Mackintosh and Koivusalo 2005; Mekee, Lehose and Nolte 2007; OECD 2997). But some areas are not examined in depth. For example, information on the distribution of scanners and MRI is available, but it is meaningless unless placed in the context of medical and clinical infrastructures (Anderson and Poullier 1999; Reinhart, Hussey and Anderson 2002), clinical trials circumstances and local service delivery structures. According to Japanese and foreign experts, the situation for regulatory clinical trials in Japan is underdeveloped in comparison to the US and EU member states.

Despite the differences between the EU countries and Japan, these two regimes share more commonalities than with the U.S. health care system. Japan and the EU member states share a similar philosophy underpinning their respective healthcare systems and the mechanisms to provide for it. Unlike the American system, Japan and the EU countries support universal coverage, contributions based on ability to pay, and benefits according to needs (table 2).

[Table 2: The Incorporation of Solidarity into Health Care]
In economic evaluations, the comparative performance of healthcare systems is usually assessed in terms of three principles: the cost of health care (efficiency), access (equity) and quality (efficacy). While these three principles are crucial, the mechanisms for coverage, reimbursement and compensation found in a particular healthcare system actually determine a patient’s ability to access innovative and advanced medical technologies. Access or service barriers are typically discussed from the perspective of cost-sharing and co-payments, the geographical and organizational barriers to care – e.g. waiting times for all kinds of general or specialized health care, elective surgery and acute emergency care, as well as diagnostic care (European Commission 2008). As discussed above, access to medical technologies is not the same as most access issues.

Access to medical technologies is not secured anywhere, not in the ‘4+1’ models found in the EU27\(^20\) nor in Japan, although they all adhere to the principle of universal access to health care. The culprits are past and on-going healthcare reforms in EU member states and Japan over the last two decades, and the dismantling of healthcare systems in Eastern Europe following the collapse of communism. In the European countries and Japan, cost containment policies and stringent controls have had priority over the closing of the service and access gap, as they have in the U.S. However, two fundamental structural differences separate the American case from the other two cases. In Japan and the European countries, global health budgets are integral parts of national budgets, and even where separate NHI budgets exist, they are subject to national politics, and cost containment decisions are made by central governments responsible to an electorate with a vested interest in healthcare matters. In contrast, the Unites States global or sectoral budgets for ambulatory and hospital care or a national global healthcare budget do not exist. Budgeting is piecemeal, highly fragmented, and results from the individual decisions of numerous commercial and public payers such as Medicare and Medicaid and the Veteran Administration. In general, the public’s attention is only triggered by rhetorical campaign speeches that inevitably die down after the election ends. In general, the American public’s interest is only piqued when responding to a crisis.

Reimbursement rates and levels result from multiple decisions made by numerous decision-making layers inside and outside the healthcare systems. These involve four clusters of mechanisms covering the (i) coding: (ii) coverage: (iii) payment for medical devices and; (iv) technology assessment (HTA). HTA was weak in Japan in the mid-1990s and continues to be weak when compared to European countries and the U.S. (Hisashige 1994; Banta et al 1994).

Decisions on these elements, together and alone, heavily influence the opportunities for marketing medical devices, earning profits and reinvesting in R&D, and influencing patient access to treatment. From the perspective of the industry, reimbursement is too low, inadequate and harmful to business and insufficient for R&D. One must keep in mind that the lucrative business aspect of healthcare is innovation, making R&D essential (Burns 2005, chs. 6-8). From the perspectives of payers (public and private alike), the hurdles are not high enough to discourage the diffusion of new and costly medical technologies into the healthcare system.
Used increasingly as a tool for cost containment by public and commercial payers, which tend to undermine patient access to novel and advanced therapies, these reimbursement methods have been the driving force behind significant health care reforms. This is the case even in otherwise equitable and universally accessible healthcare systems in Europe and Japan. These effects are obtained through the exclusion of certain devices and procedures from the benefit package, increased copayments, and in Japan by the notorious “medical device gap” (the industry preferably refers to a “product gap”). A “device lag” is understood in Japan as medical devices and IVDs which are used in other advanced societies but not yet approved in Japan. This “device lag” is acute in oncology, cardiovascular diseases and orthopedics, but the term “device lag” also stands for the “off-label” use of devices for indications for which they are not approved. The “off-label” use seems to be particularly acute in Japan but is also present in the U.S. and Europe (Swiontkowski 2007). This high “off-label” use in Japan can be explained by the weak controls on Japanese physicians’ and lax government controls on medical institutions. By contrast, professional controls on American and European physicians and medical facilities are more extensive than they are in Japan. 

Four generic forms of medical device reimbursement are used alone or in complex combinations – (i) product reimbursement; (ii) physician reimbursement; (iii) surgical intervention reimbursement and; (iv) DRG-based payments and in Japan DCPs (Diagnostic Combination Procedures). The move towards DRG-based payment approaches for in-patient care is recent and reflects a global trend. Two forces are at work in regard to DRG-based reimbursement: “governments are trying to concentrate DRG groupings; and the medical technology industry is trying to expand them” (Rosenbloom et al. 2007: 51; Clinica # 1322, 2008: 68). Obviously, companies who want reimbursement for their products must lobby for the inclusion in the DRG-listing while payers directly or indirectly have increasingly insisted on an assessment of the efficacy/effectiveness of the new technology. Payers demand clinical evidence and economic data for manufacturers’ claim of medical efficacy of their products. Payers are concerned about two issues: (i) does a new device add therapeutic value over existing treatments and is the likely outcome of using a new product or procedure on a patient improved compared to an older treatment or product and; (ii) does it offer value for money?

Access to medical technologies is managed through cost controls but they vary from country to country. Experts agree that “the points of control start with the regulatory process in Japan while the U.S. points of control start with reimbursement.” In Japan, an extraordinarily complex review and approval process combined with “an undifferentiated health care system” (Ikegami and Campbell 1999: 59) helps to delay and slow down the introduction of costly novel technologies into the Japanese healthcare system. This system also explains why patients in Japan tend to have access to certain technologies years later than European and American patients. The European Union has “one stop for regulation but 25 stops for reimbursement” (see table 3). As Rosenbloom et al note, “Throughout Europe there are few regulatory hurdles, but rising reimbursement hurdles.” In the future reimbursement hurdles are likely to increase, as
healthcare reform has become a never ending process in the advanced world. Additionally, Rosenbloom et al (2007: 46) add, “Reimbursement is used politically as a means of price curbing and slowing access to the latest technology, which leads to frequent overhauls of the systems in an attempt at achieving the best value for money.”

In Europe, reimbursement schemes vary from one country to another. They differ for private and public health care and may differ from product category to product category. Reimbursement can also differ from region to region within one country.

[Table 3 DRGs in Five Selected European Countries]

The overall approach to patient group systems follows international developments in disease classifications. For example, France, Germany and the United Kingdom follow patient groupings using the ICD-10 (10th revision, but others use ICD-9), adjusting them to the particularities of their healthcare system. France and the UK require technology assessment in health care (HTA) as a precondition for inclusion in the catalogue of reimbursable items. In France and the UK, an assessment by the authorities is the norm and precedes the application for reimbursement. In contrast, if German companies accurately code and group products into an appropriate DRG that is paid enough to cover the hospital’s costs, they can place with relative ease new devices on the German market. DRG schemes in the U.S. and Europe, as well as the Japanese equivalents (DCPs), are designed to improve the cost-effectiveness and overall efficiency in delivering health services but the DRG system creates numerous problems for the patient, such as encouraging payers to select a cheaper device if possible or discharging “quicker and sicker” patients when trying to reduce the length of patient stay.

In Japan, the basic structure and issues concerning stakeholders’ pricing and reimbursement have not changed since the 1990s, nor have the two-year reviews of prices and costs and the related cuts in reimbursement rates, or the up/downgrading of functional categories (Campbell and Ikegami 1998). Although the MHLW remains the “single national access point for coverage and reimbursement of all new medical technology” (Rosenbloom et al 2007: 113) in April 2008 MHLW finally adopted new reimbursement rules designed to expedite access for Japanese patients to some devices which are to be reimbursed at a higher rate.25

Acutely aware of a “device lag” and under immense political pressures from the government’s program on Innovation 25 and the Five-Year Strategy for Creation of Innovative Drugs and Medical Devices, MHLW established two groups in 2006: a selection working group (WG) and a study evaluation group (SG), responsible for putting together a list of highly needed medical devices to be imported in Japan. Upon request by the Medical Device Evaluation Office, and supported by the Health Policy Bureau (HPB), Japanese medical and academic societies were asked to submit a prioritized list of “highly needed medical devices.” In a step-by-step process, medical devices were ranked and prioritized according to two criteria: “highly medically needed” and “disease severity.” Originally, in October 2006, MHLW intended to approve five or six kinds of
medical devices, but by January the priority list included thirteen candidates. These must meet three criteria: (i) offer a medical benefit to patients suffering from a life threatening disease; (ii) have a major impact on daily living of patients suffering from a life threatening disease; and; (iii) provide a treatment of diseases for which treatments are currently not available in Japan. MHLW asked the industry – Japanese and foreign – to submit applications for “highly needed medical devices.” The candidates that survived this step-by-step process are subject to a “fast track” review and approval process.

To further narrow the access gap of Japanese patients to innovative technologies in December 2008, MHLW announced an *Action Program for Speedy Review of Medical Devices* designed to reduce “the time to approval of medical devices, including efforts at accelerating the processes for the review of medical devices, by taking scientific and reasonable measures in a positive manner.” The plan is to increase the number of qualified and better trained reviewers, start a three-track review system (for new medical devices, improved medical devices, and me-too medical devices) and clarify the review criteria, as well as disclose information. These administrative measure are meant to put PMDA and MHLW in a position that they concentrate their money and staff resources on the much medically needed high risk-devices while transferring all Class II medical devices to the certification system by third party (i.e. commercial) certification bodies (Yaginuma 2009).

The current efforts have been set off by the repeated and often heavy handed pressures of commercial diplomacy involving senior Japanese and U.S. government level officials, including the U.S. embassy in Tokyo, U.S. trade representatives, and the powerful lobbying strategies of the ACCJ (American Chamber of Commerce Tokyo), AdvaMed and individual U.S. companies in Tokyo. Rather than being a new phenomenon, a strong American presence in Japan goes back to the mid-1980s, when in order to avoid a trade war, the U.S. and Japan initiated the so-called MOSS talks or market-oriented, sector selective talks. The pharmaceutical sector was selected and, by default, the medical device sector. Since then, meetings of the U.S. industry and the Japanese government take place once a year (called a *Teikikaigo*). Participants from the Japanese government include HIB, PMDA, Economic Affairs Divisions within HPB. U.S. industry is represented by JMFDA, the Imaging sector and the IVD sector, as well as the ACCJ and the EBC.

In summary, from the medical device industry’s perspective, reimbursement could always be higher for R&D. But reimbursement levels need to be balanced against the objectives of the healthcare system to provide affordable, equitable and solidarity-based universal health care. From a payer’s perspective (public and commercial alike), the hurdles are not high enough to discourage the diffusion of new and costly medical technologies into the healthcare system. Used increasingly as a tool for cost containment by public and commercial payers, these reimbursement methods represent significant obstacles for patients in need of novel and advanced therapies. From a patient’s perspective, access to medical technologies is a huge challenge, with the patient’s physician/s largely responsible for one’s healthcare success and recovery.
Concluding Comments: Lessons from the Comparison

Although admittedly a preliminary account, this paper addresses key regulatory issues, explains why they are significant, and why the common structural features of the regulatory regime warrant a close examination by the social science research community. The paper also briefly summarizes the nascent foundations of a medical device regulatory regime by drawing on each case study’s respective medical device regulation history and their various medical device reimbursement approaches. Despite its preliminary nature, the three cases taken together reveal compelling observations concerning the emerging balance between global and local dynamics, and the political and health risks involved when regulating medical devices for consumption on a local and global level. While the internationalization of regulatory affairs and some convergence across the three cases are beyond any doubt, the findings so far do not support the proponents of globalization who proclaim a declining role for the nation-state and, by extension, national authorities.

The internationalization of regulating medical devices has been driven by extraordinarily complex and mutually reinforcing developments. The first developments concern the rapid and revolutionary advances in several scientific disciplines, new applications of medicine and new treatments, as well as their diffusion into the respective national health care system. Whether patients benefit from these advances and medical innovations depend on the clinical infrastructures, clinical expertise, training and research resources available. Unlike Europeans and Americans, the Japanese have not fully benefited from these advances, nor have they benefited from advanced life-saving and life-enhancing medical technologies (with one noticeable exception: progress in tissue and cell engineering). While Japanese patients have universal access to health care through NHI, they have limited access to a broad range of medical treatments and treatments of high quality due to highly bureaucratic, lengthy and delayed approvals of new medical devices. Ironically, the high quality and state-of-the-art technology that made the Japanese electronic industry so famous is not replicated in the health care sector. Unlike their European and American colleagues, Japanese medical specialists with few exceptions appear not to have been the drivers of medical innovations. Nor do Japanese clinical research infrastructures do not operate at a level comparable to biomedical research projects and multi-site clinical trials in Europe or the U.S.

The GHTF - the only global forum for the medical device sector where bottom-up and top-down processes are going on simultaneously - has made modest progress over the last fifteen years toward establishing a global regulatory model, with an emphasis on pre-market requirements. But it is difficult to compare its current progress with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in terms of the legal status and binding rules. True, the GHTF is moving in that direction but has a long way to go. And due to the heterogeneous nature of medical devices and medicine, in which both the practice and training for medicine and delivering care are embedded in divergent national and local cultures, this “single window” may not be realized in all regulatory matters leaving room for national discretion – perhaps not such a bad thing when taking the interests of the consumers and patients into consideration.
As a consequence of global trade and the internationalization of regulatory affairs, the relations between two groups of stakeholders have become ever more intimate despite the political demand for legal transparency. The first group of stakeholders, operating at the global and national levels, are the members of the “troika” of vested interests – regulators, trade associations, the medtech industry and individual global companies. They frame the issues and set the global regulatory agenda. The second group of stakeholders operates at the micro-level and includes device makers, clinical researchers and surgeons. Both stakeholder groups are surrounded by a wall of silence that greatly curtails transparency. However, it is the medical profession’s complicity with the medtech industry and global device companies that is becoming more troublesome.

The European Union, Japan and the United States, together with Canada and Australia, represent the founding member countries of the GHTF. Since the early 1990s, each country and the EU have actively participated in global efforts promoting the GHTF’s objectives, but as Drezner argues, empirical data indicate that the great powers – the U.S. and the EU – remain the key players in writing global regulations and their power is due to the size of their internal economic markets. It was in their interest to design the GHTF as a voluntary body, while retaining domestic controls over the healthcare market, the delivery of health care and the existing power structures. Furthermore, it proves advantageous to find solutions based on their practices without having to engage in domestic legislative changes and to curb or stabilize spending on health (public and private).

Japan, lagging behind the two western regulatory regimes and intent on catching up, has used global agreements on standardized documents such as STED (the Summary of Technical Documentation) as a justification for domestic legislative changes. Due to too many change-resistant agents in the political, administrative and professional realm impacting the regulation and delivery of health care in Japan, these legislative changes may never have come about without this external stimulus. Japan’s regulatory approach borrows elements from the U.S. and the EU regimes. From the U.S., Japan borrowed the idea that governmental controls through the FDA are best. While retaining many home grown features, or what foreign observers call “the idiosyncratic” features of the Japanese approach to regulation and health care, Japan also borrowed the EU idea of nongovernmental third party certification for lower risk devices and the format for adverse event reporting (AER). Doing so created a labyrinth of implied contradictions distinguishing government control through the FDA and MHLW and the non-governmental certification process at the EU level.

These three regulatory-regimes share a number of common structural features, all of which have serious implications for patient safety issues. For example, despite the application of the “life cycle concept” covering pre-market and post-market surveillance regulatory tasks, attention is drawn to the pre-market approval process — a highly respected practice within the producer and advocate communities favoring a competitive industry. The current understanding among regulators predominantly tends to be reactive rather than proactive. As the chair of GHTF’s SG5 Clinical Evaluation and chair of a
related EU Task Force Dr. Susanne Ludgate, Clinical Director of the Medicines and Healthcare Products Regulatory Agency in the UK argued: “We need systems for the timely availability of safe and effective technologies to patients and practitioners underpinned by streamlined regulatory processes in the best interests of public health.” This orientation does not sit too well with the industry solely interested in least burdensome regulation.

Unlike the drug sector, the medical device sector for a long time has been successful in avoiding the radar screen of scrutiny by the public and the media, despite the fact that recalls of high-risk devices are as frequent as drug recalls. The regulatory agencies - FDA, the European and Japanese quasi-independent regulatory agencies – depend on intramural and extramural scientific advice. This dependence has brought to the fore potential and empirical confirmed conflicts of interest between device-maker and surgeons, device makers and purchasing agents (health facilities), and lobbyists and policymakers. The borderline between legitimate and illegitimate influences is fluid, and conflicts of interest issues only recently began receiving attention from both the media and the public. Who controls the regulators? The alarming economic dependence of the regulatory agencies on user fees paid by the device makers to carry out their regulatory responsibilities seems to provide an interim though not exhaustive answer.

The regulatory regimes are perceived to be strongly rule-based, formalized, and, in the U.S. case, extremely legalistic, emphasizing how law and procedures trump patients’ interests. From a comparative perspective, it appears that they are equally formal and rigid, with each regulatory agency’s overall capacity depending upon who can access foreign markets. For example, many U.S. companies, wishing to enter the Japanese market, often complain about the Japanese bureaucracy’s (MHLW and PMDA) strict adherence to following process and procedure (e.g. insisting that changes in packaging and coloring be reported rather than emphasizing safety-related issues when submitting applications for market approval). Similar complaints but possibly for different reasons are heard from foreign companies seeking access to the U.S. market. By contrast, U.S. device makers highly value the perceived ease of entry to the EU market based on EU certification through CE marking by third party non-governmental certifiers. This may be changing in the future, as the European Commission tightens rules for high risk devices and advanced therapies, and that global regulators work toward a ‘global model’.

While global trade is pushing regulatory issues onto the global stage favoring market approvals over concerns for aftermarket patient safety and clinical trial issues, governments and payers have kept reimbursement – covering the coding, coverage, reimbursement of medical devices and technology assessment in health care (HTA) — close to their chest under national controls. Reimbursement concerns are the most local and least globalized aspects of the entire comparative research project. The findings speak to serious and consequential lack of domestic policy coordination between the regulatory authorities, those who check on quality assurance and evidence-based medicine through HTA, and those responsible for the delivery of health care. Organizational autonomy, public and private competition for prestige, client control over
specific channels and access to policymakers, inertia and turf protection, etc. are among the many status-quo inhibitors of better coordination of regulatory policy and health policy and striking a better balance between the interests of patients and those of business.

Will the internationalization of regulatory affairs and the ever increasing product differentiation within both the medical device and information technology sector facilitate a move toward global and regional convergence? Or will features unique to each country-specific regulatory and healthcare system, including the medical research capabilities, be reinforced? We hope to have some answers at the completion of this project. In addition, only time will tell what role the GHTF will play in actually improving global patient safety standards. The jury is not in and the issue remains wide open. Meanwhile, national regulators will remain in firm control over the regulatory functions and delivery of medical care in their respective countries.
Table 1: Highlights of medical devices for the United States, EU, and Japan

<table>
<thead>
<tr>
<th>Medical devices</th>
<th>United States</th>
<th>EU</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Production</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global share</td>
<td>51%</td>
<td>30%</td>
<td>10%</td>
</tr>
<tr>
<td>Value (2005)</td>
<td>$92.0 billion</td>
<td>$38.0 billion</td>
<td>$14.2 billion (2004)</td>
</tr>
<tr>
<td>Dominant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>products</td>
<td>- Interventional cardiology (coronary stents, pacemakers, defibrillators)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Diagnostic imaging</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Orthopedic implants</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Patient monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Medical and surgical instruments</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- In vitro diagnostics (IVD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Consumption</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global share</td>
<td>50%</td>
<td>30%</td>
<td>10%</td>
</tr>
<tr>
<td>Value (2005)</td>
<td>$90.2 billion</td>
<td>$38.1 billion</td>
<td>$19.0 billion (2004)</td>
</tr>
<tr>
<td>Population</td>
<td>298.4 million</td>
<td>457.0 million</td>
<td>127.5 million</td>
</tr>
<tr>
<td><strong>Trade balance (2005)</strong></td>
<td>$1.8 billion</td>
<td>$4.5 billion</td>
<td>$-4.9 billion (2004)</td>
</tr>
<tr>
<td><strong>Total Employment (2005)</strong></td>
<td>388,4 million</td>
<td>393,000</td>
<td>68,000</td>
</tr>
<tr>
<td><strong>National Healthcare Expenditures (percent in GDP)</strong></td>
<td>15%</td>
<td>7-8%</td>
<td>8%</td>
</tr>
<tr>
<td><strong>Research &amp; Development Expenditures</strong></td>
<td>10-13%</td>
<td>6%</td>
<td>6%</td>
</tr>
</tbody>
</table>

* Reported R&D expenditures as a share of sales.
Figure 1: CDHR PMS Transformation Connecting the Dots

### Table 2: The Institutionalization of Solidarity into Health Care

<table>
<thead>
<tr>
<th>Integration into the system:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• inclusion of all citizens (universality);</td>
</tr>
<tr>
<td>• mandatory affiliation for the citizen (prohibiting opting-out from the statutory scheme), requiring his/her financial participation in the public system;</td>
</tr>
<tr>
<td>• an obligation of acceptance of the administering bodies (prohibition of exclusion).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Funding:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• a progressive income-related contribution;</td>
</tr>
<tr>
<td>• a contribution independent of individual risk factors (i.e. medical history, age, sex);</td>
</tr>
<tr>
<td>• cross-subsidization among schemes.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• equal treatment for equal need;</td>
</tr>
<tr>
<td>• progress cover according to needs (positive discrimination in favor of those in greatest need)</td>
</tr>
</tbody>
</table>

Table 3: DRGs in five selected European countries

<table>
<thead>
<tr>
<th></th>
<th>France</th>
<th>Germany</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>How many DRGs?</td>
<td>783, of which 84 ambulatory</td>
<td>1,082</td>
<td>522</td>
<td>828</td>
<td>609</td>
</tr>
<tr>
<td>When were DRGs introduced?</td>
<td>1995 in public hospitals</td>
<td>2004 (obligatory for all hospitals</td>
<td>1994 Note 1</td>
<td>Early 1990s</td>
<td></td>
</tr>
<tr>
<td>What is the update procedure?</td>
<td>Public agency (HAS/ATIH) Updates algorithm regularly</td>
<td>Annual recalculation</td>
<td>Note 2</td>
<td>Unclear</td>
<td>Annual recalculation</td>
</tr>
<tr>
<td>Are medical procedures covered?</td>
<td>Procedures are covered in tariffs</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, within DRGs</td>
<td>Annual recalculation</td>
</tr>
<tr>
<td>Are outpatient procedures covered?</td>
<td>‘ambulatory’ yes; outpatient no</td>
<td>No</td>
<td>No, outpatient services are listed in the ambulatory list</td>
<td>No</td>
<td>Some, e.g rehabilitation</td>
</tr>
<tr>
<td>Are diagnostic procedures covered?</td>
<td>Yes, but differences according to systems</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, within DRG</td>
<td>Some, Eg diagnostic imaging</td>
</tr>
<tr>
<td>Are tests covered?</td>
<td>Idem</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, within DRGs</td>
<td>Some</td>
</tr>
<tr>
<td>Do minimum stay requirements apply?</td>
<td>Not really, But ambulatory if length of stay less than 48 No really,</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Apply to day case and inpatients</td>
</tr>
<tr>
<td>Are additional payments possible Eg top ups?</td>
<td>High outliers MDs ‘en sus’ payments</td>
<td>Yes, eg innovation or supplemental</td>
<td>Not in principle</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

Endnotes


3 The term medical device stands for a huge spectrum of medical technologies that vary widely. This paper uses the term medical devices and medical technologies interchangeably.

4 A more detailed historical account of forces such as the widely observed “agencification” is in progress, as is an in-depth monograph on each of the three cases.

4 The FDA defines diagnostic products as any “in vitro reagent or other related article, including any component, part, or accessory, which is intended for use in the diagnosis of disease” (Federal Food, Drug, and Cosmetic Act (FD&C Act) sect. 201(h)). But novel and highly sophisticated diagnostic technology in genetic testing and biotechnology are challenging a hands-off position of the FDA.

5 Along similar lines, the FDA launched a pilot project with Japan – called “Japan-U.S. Harmonization by Doing”...to allow availability of novel treatments and innovative, safe and effective medical devices to patients more quickly” *HBD Pilot Program Initiative* (FDA website accessed 1/08/08).

6 A rigorous analysis of R&D funding of advanced medical technology is outstanding, as is a study of the nefarious impact of industry money on the scientific and medical research process. The contracting out of research functions to for-profit research organizations or clinical research organizations (CROs) in the three regions is a topic for future research. According to medical device experts, the problems of lack of accountability and conflicts of interests tend to be more serious and more frequent than in the drug sector, as summarized by Angell 2005 and Petersen 2008.

7 In a three-country comparison –the U.S., Germany and Switzerland – Robert Kaiser provides the empirical data to show how non-market-incentives provided the head start for innovation and eventual commercialization of the U.S. pharmaceutical biotechnology industry. The German and Swiss industries did not benefit from such advantages.

8 Efficacy means that a medical device can be shown by valid scientific evidence to produce an intended clinical effect in ideal circumstances while effectiveness of a medical device stands for intended clinical effects under routine circumstances.

9 Examples of combination products are drug pre-filled syringes, drug eluting patches, drug eluting stents, heparin-coated catheters; a combination product can also be a co-packed product, such as a surgical kit containing catheters, rubbing alcohol, etc.

10 Co-regulation comes in various forms and reflects a pattern of business-government relations characteristic of European countries. By contrast, the concept self-regulation reflects the well known distrust of the state and government by U.S. business. These fundamental differences in culture, history and institutions are viewed as root cause of a paradox emerging from the field research which requires in-depth scrutiny. National regulators cooperate through the Global Harmonization Task Force and produce harmonization documents. When they get back to their home base, they admit themselves that “they ignore the GHTF documents.” The exception to the rule is Japan which institutionalized the STED into national legislation. Insiders speak to a formidable “cat and mouse game between the FDA and the European Union regulator.” As another insider said: the FDA has been the leader in medical device regulation historically but is increasingly isolated among the regulators around the globe who tend to favor mutual recognition agreements (MRAs) or memorandum of understanding (MoU) with the EU while the FDA is viewed as favoring a bi-lateral approach.
The issue of independent certification bodies or notified bodies, which are commercial entities, could be an exception to this claim.

Ulrich Dolata draws a useful distinction between “the sectoral adaptive capacity of new technologies” and “the sectoral adaptability of socio-economic structures, institutions and actors confronted with the opportunities presented by the new technologies.”

For simplicity sake, at this stage we use both concepts interchangeably.

The approval of class II devices (including some 820 medical devices and 370 IVD reagents) through a third party is a novelty in Japan and a response to the criticism of cumbersome and unnecessary government regulation.

RAJ Devices, the leading regulatory journal for regulatory professionals writes in the February issue 2008. A review of recent direct-to-consumer advertisements for implantable devices found they lacked basic information about side-effects” (italics in original).

We will leave unanswered the question whether the FDA can or should serve as reference for international comparison.

In the U.S. 2009 presidential primaries the contributions to the candidates (Republicans and Democrats alike) have exceeded the campaign funds of the drug industry!

The observations about the stage of medical innovation in Japan came as a surprise. In comparative research of advanced industrialized nations it is standard practice to include Japan. Yet, the high quality and state-of-the-art-technology that have made the Japanese industry famous is not replicated in the healthcare sector. It is true that Japan has the highest number of MRI units and CT scanners, even higher than the U.S. per million population. Focusing on the distribution of hardware rather than the software of clinical practice can be misleading, especially when taken out of context.

Professor Arakawa heads the Clinical Research Center, Tokyo University Hospital. In 2006, together with six other university hospitals they launched for the first time a “University Hospital Clinical Trial Alliance (UHTC Alliance), a voluntary group of university hospital clinical trial offices to improve Japanese clinical trial environment and implement multinational clinical trials safety and efficiently.”

This formula reflects the current state of the art in the welfare state literature building on Esping-Andersen’s (1990) original argument concerning the existence of three distinct regime types underlying European welfare state developments and, by extension, healthcare systems. Building on Esping-Andersen’s influential work, Stephan Leibfried (1992) distinguished between four social (health) policy regimes: The Scandinavian welfare states, the ‘Bismarckian’ countries in Continental Europe, the Anglo-Saxon countries and the Mediterranean or Latin Rim countries. With the collapse of communism in Central and Eastern Europe, a new mix of solidarity-based and for-profit healthcare system evolved.

The literature on professional governance and hospital policy and management is too extensive to be reviewed here.

Professor Naoki Ikegami’s presentation on the Japanese and Dr. Paul Ginsburg’s presentation on the U.S. health care system at the International Conference sponsored by the Medical Technology Leadership Forum (MTLF) in Karuizawa, Japan, April 21-23, 2007, and their moderation and discussion.

Phrase used by an industry source at the MTLF.

Rosenbloom et al., op.cit., p. 46.

The 2008 changes are not yet examined.

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