Medical device regulations as a source of industrial leadership
A comparative study of American and European regulatory approaches

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Abstract

Medical technology industry which produces the whole range of medical devices from eye droppers to computer tomography scanners is characterized by serious learning problems of industry stakeholders due to its high technological complexity and product diversity. Majority of firms populating the sector are small companies with no revenues, and therefore, depending strongly on venture capital to get their products on the market. At the same time due to technologies which are successfully launched, this industry employs highly qualified staff, promotes jobs and tax revenues. The industry progress is fueled by process of incremental innovation which occasionally produces technological breakthroughs.

Medical device regulations, i.e. the mechanism of granting by a state to a manufacturer the rights to market her products in return of proof of their safety and effectiveness/performance, are an important element of innovation ecosystem of medical technology industry. They serve as a tool for decreasing uncertainty of stakeholders' interactions on the market, ensuring public safety and legitimacy for manufacturers and their products. Supportive medical device regulations improve investment climate in the industry by reducing related risks, and, hence, contribute to promotion of innovation in the short run and better and cheaper healthcare in the long run. In the regional context, therefore, particular design of medical devise regulations can be a source of competitive advantage of the whole region in the international arena.

The present study compares two dominant regulatory frameworks: American and European. It attempts to answer the question: Which specific features of national/regional medical device regulations contribute to sustaining or improvement of a current and future position of a country/region on a world leadership chart?

The two approaches are studied at present as well as in dynamics, the parameters determining the regulatory approach success are pointed out and then specific traits of regulatory approaches underpinning success parameters are defined and conjectures are made regarding the future trends of development for each of the two approaches. It has been shown that U.S. and EU regulatory frameworks are likely to ensure similarly high safety level of devices, while European approach seems more efficient. Such traits
of European framework as use of international performance standards and diversified responsibility among actors involved into regulatory process contribute to its higher efficiency.

**Key-words:** medical device, regulations, US, EU, industrial leadership
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1 Introduction

Medical devices in general sense represent a wide and diverse group of equipment used for "mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals" (FDA, 2011-1) but different from pharmaceuticals in terms of way they interact with the body. While pharmaceuticals prime mode of action is achieved by chemical means or metabolizing of a medicine by the body, medical device acts through other ways of interaction with a patient, i.e. physico-chemical, physical, mechanical or others. Medical devices vary from simple ones which we use in our homes, such as eyedropper, to very complex units to be used by specially trained professionals in a hospital environment, such as computer tomography scanners. The corresponding industry developing and producing medical devices is called medical technology industry and often abbreviated as “medtech”.

Since the beginning of its rapid growth in 1980s medical technology has made a remarkable contribution to improvement of public health and overall quality of life (Makower J., Meer A., Denend L., 2010) by introduction of new diagnostic techniques and devices which serve as aide in therapy. Improved outcomes for patients with such economically demanding conditions as cardiovascular diseases and diabetes type II have contributed to reducing death and disability rates and providing direct savings for the economy (MEDTAP International, 2004). Medical technology industry positively impacts the region’s economy in whole as well, promoting jobs and tax revenues (Lewin Group, Inc., 2010) and, e.g., is one of the few industries in the US, where export exceeds import.

In the course of the economic activities’ development the complexity and uncertainty of their actors’ interactions rise and effective institutions reducing this uncertainty and the transaction costs of human exchange are required (North D., 1990). Medtech is a technologically complex and rapidly innovating industry, i.e. users of the products of this industry cannot fully grasp their technological background and compare effectively different products’ quality and functionality, i.e. experience serious learning problems (Carpenter D., 2010). In such an industry, therefore, the transaction costs of human exchange are especially high and the need in mediating institutions which would enable the technologies to diffuse should be especially urgent in this industry (North D., 1990).

Moreover, in case of Medtech such institutions as entry or approval regulations create the very possibility of a market to exist (Carpenter D., 2010). This mechanism is applied on national level in many countries as well as on the international level (Cheng M., 2003) and based upon requirements to the devices’ safety and effectiveness/performance. Manufacturers must comply with these requirements in order to get an access to the market, i.e. regulations in medtech provide the manufacturer with necessary legitimacy (Hiderfjäll, 2010).

Not only manufacturers compete for market share, the countries and regions compete for global industrial leadership as well (Mowery D., Nelson R., 1999). Different countries and regions of the world have different abilities to take advantage of technological advancement in the industry, so that their share of the global market would grow (Coriat B., Malerba F., Montobbio F., 2004). According to opinion leaders in the industry (PwC 2011, Makower J., Meer A., Denend L., 2010), regulatory environment is one of the key factors of development of such a technology-intensive industry as medical devices. Effective regulatory framework is able to contribute to the country’s or region’s innovative
capacity, which, in its turn, defines the pattern of the global industrial leadership in the industry.

Medical technology and its regulatory aspect have been rather underserved with regards to academic studies so far. Sources of industrial leadership are discussed for diagnostic imaging devices (subgroup under medical devices) in the work of Annetine Gelijns and Nathan Rosenberg (1999). The regulatory environment has been touched upon very shortly in their work. Patrik Hiderfjäll (2010) discusses the institutional dimension of medical technology innovation system as an important element of the industry environment, although, not going deep into discussion of specific traits of effective regulatory framework. Keeping in mind empirical data mentioned before, it would be appropriate to expand the research in this direction.

Therefore, it is of interest to assess the regulations in the wide geographical context and time span, as a tool for management of markets and formation of the future innovative landscape in medtech. Especially intriguing in this context seems the task of comparison of the regulatory approaches adopted in the United States, the global leader in medtech innovation and its closest follower, European Union. The US and EU are the two largest markets as well as producers of medical devices in the world (Cheng M., 2003, Lewin Group, Inc., 2010). Furthermore, the present moment is a high time to conduct such a study, keeping in mind the concerning signals coming from the industry (Makower J., Meer A., Denend L., 2010) which suggest that the regulatory environment in the US has been getting less supportive for innovations recently, which, in its turn, might shift the attention of the industry to Europe, compromising the leadership positions of the US.

The research question of the present study is:

Which specific features of national/regional medical device regulations contribute to sustaining or improvement of a current and future position of a country/region on a world leadership chart (using examples of US and EU regulatory approaches)?

The goals of the study are to:

- Describe the current regulatory approaches applied to medical devices in the US and EU and point out their fundamental similarities and differences (addressed in Chapter 4),
- Define causes and direction of change of medical device regulations both in the US and EU (addressed in Chapter 5),
- Assess performance of medical device regulations in the US and EU (addressed in Chapter 6),
- Point out factors which are of importance now to determine future effectiveness of both regulatory approaches, and, subsequently, defining the perspectives of sustaining or improvement of international competitiveness of respective industries and markets (Discussed in Chapter 7 on the base of analysis performed in chapters 4, 5 and 6).
2 Study methodology

The theoretical base for the present topic has connections to different branches of social, political and economic knowledge. Due to this interdisciplinary character of theoretical field the study relates as well as the topic’s nature, an interpretive scientific approach and an inductive method of linking theory with empirical material are applied to it, as it is not possible in this setting to build a hypothesis to be proved basing on unambiguously preset theoretical assumptions. Therefore, empirical material is a point of departure of the study and its description and analysis serve as a base for generalization.

Qualitative method of analysis is applied, as the research question of the present study calls for finding objective similarities and differences in various aspects of the two approaches compared, rather that measuring their magnitudes. Analysis instruments applied in the study depart from applicable frameworks proposed by Daniel Carpenter (2010), a combination of those given in two works of Mary O. Furner (2010) and her earlier study together with Barry Supple (1990) as well as in the work of Douglas C. North (1990).

Static as well as dynamic view on medical device regulations is presented. Combination of both is going to indicate the possible future trends in this area.

In order to achieve the study goals the following analysis will be performed:

In the Chapter 4 both regulatory approaches will be described and then studied at the present time in a way which enables to highlight the differences between two regulatory systems. Specific features of clearance/approval process on both markets will be analyzed, as referring to D. Carpenter’s opinion (2010) which suggests that this process is a key element in forming the current industry state. While the analysis was carried out it appeared to be appropriate to describe also two elements of regulatory system supporting the process of approval: responsibilities of the actors involved in the two systems, and corresponding legal frameworks.

After that the US and EU regulatory systems will be studied in dynamics:

First, in the Chapter 5, causes and direction of change of medical device regulations both in the US and EU will be discussed. Analysis will be performed according to a set of factors defining the formation of both ideas and practice of the regulatory traditions (Furner M, Supple B., 1990; Furner M., 2010), i.e., relevant professional and practical knowledge, beliefs and values prevalent in the society legitimating policy making; specific predetermined paths of regulatory institutions development; and specific national/regional patterns of interactions of the society and the state.

After that, in the Chapter 6 both US and European frameworks will be assessed according to parameters which determine effective functioning of institutions and its dynamics (North D., 1990), i.e. stakeholders of regulations, their relative motivation and ability to measure and reinforce the desired path of regulation’s evolution, as well as evolution of environment complexity will be described. The factors which determine effectiveness of national/regional regulations, according to these observations, will be pointed out. The data suggesting the resulting effectiveness and efficiency of both American and European regulations will be presented, according to multiple industry reports.
The factors which are of importance now for a regulatory approach’s current and future competitiveness will be defined by combining the results of applying the research tools mentioned above, in Chapter 7.

This study is based on the analysis of publications containing both primary empirical material (laws, guidelines and other information published on official websites of American and European authorities) as well as secondary empirical material. Secondary sources include articles and reports providing interpretations of law and industry studies. The reports produced by such consulting agencies as PricewaterhouseCoopers and Boston Consulting Group, to name a few, are based on solid research methodologies and thorough collection of empirical material. Other reports, such as the study performed by Josh Makower et. al., and articles interpreting laws and guidelines published in industry journals such as IVD Technology or Medical Device and Diagnostic Industry Magazine are written by industry and regulatory professionals with deep experience concerning related regulatory issues. Therefore, these sources are viewed as valid for this study.

Among limitations of the present study the greater availability of information on the American regulatory system compared to European one should be mentioned. European approach is much younger than the American one; moreover, due to the current crisis of the US medical device regulation system plenty of reports have been issued during 2010-2011. As a consequence the emphasis and focus of the analysis may seem a bit shifted towards the US approach.
3 Theoretical discussion

3.1 Industrial performance of regional economies in the global arena: sectoral systems of innovation

The term *industrial leadership* refers to the abilities of countries to enlarge their relative shares of the global market in a given industrial sector by taking advantage of innovative technologies (Mowery D., Nelson R., 1999; Coriat B., Malerba F., Montobbio F., 2004). This notion is limited by the industries innovating mainly on the analytical level, where technological advancement can be translated into competitive advantage of firms (Mowery D., Nelson R., 1999), which is the case with medical technology industry (Hiderfjäll P., 1997).

Studies of causes and dynamics of countries’ relative industrial strength depart from rich empirical evidence collected across different industrial sectors (pharmaceuticals, information technologies, chemicals and others) as well as regions (including US and Europe) over time (Malerba, F. 2002). These findings suggest that the factors determining the performance can be found both within the firms as well as their environments. More specifically, success of technological innovation’s translation into industrial leadership depends upon high heterogeneity of firm’s knowledge and their ability to learn, i.e., on how well the knowledge specific to the sector is gained and reproduced (Coriat B., Malerba F., Montobbio F., 2004). Learning is a complex process, diffusion and preserving of knowledge involves a wide range of interactions between firms as well as non-firm organizations. This assumes that neither statical models offered by classical industrial economics nor case studies on single dimensions of sectors would be enough to make sense of the issue and one needs to apply a multidimensional, dynamical and holistic view (Malerba F., 2002).

As F. Malerba points out in his review: Sectoral systems of innovation and production (2002), the traditional notion of sector as a system constituted mainly by firms should be expanded to a wider set of specific elements. Such elements fall into three key categories: 1) *knowledge and technologies*, 2) *actors and networks* and 3) *institutions*, which altogether determine the innovation patterns specific to the given sector and its dynamics (Malerba F., 2004).

Importantly, the respective parameters of these elements are shown to be similar across one sector and different among different sectors (Malerba, 2002). Therefore, the theoretical framework which takes into account all these elements as a complex whole would define each sector unambiguously. Such framework is called *sectoral system of innovation* and serves as a suitable unit of research when the patterns of innovation and dynamics of a given sector are under investigation. Furthermore, differences in innovation patterns exist among different sectoral systems and similarities – among countries (Ibid). Therefore, comparing same parameters across regions is a relevant technique to determine sectoral variations across countries and allows assessing the range of approaches, from the least to the most successful, across national borders and over time.

Research available on industrial leadership with regards to medical technology industry is represented by the work of Annetine Gelijns and Nathan Rosenberg (1999), a thorough empirical study of diagnostic imaging sector. Factors influencing success of US, EU and Japan in gaining market share are named in the study and include links between medical research centers and universities, demography aspects (such as disease prevalence), institutional environment etc. Institutions discussed include venture capital, intellectual
property rights, healthcare system infrastructure. It is mentioned in the work that regulatory approaches have definitely an impact on the country/region success on the global market. Here, authors view entry regulations and reimbursement policies together in one section, with the main emphasis on the latter, arguing that American approach has been the most successful due to loose reimbursement and entry regulation schemes at the time when diagnostic imaging devices got to the market. However, it is further mentioned in the work that there are data suggesting that strict policy of Food and Drug Administration regarding regulation of entry leads to advantage of the US by providing incentive to the industry to strive for superior quality of products.

Although the industrial leadership patterns mentioned in the work with regards to diagnostic imaging sector can be a general guide for the industry in whole, which can be seen if we compare them to the framework used in the recent study by Pricewaterhouse Coopers (2011), the impact that regulations of entry have on medical device industry seems much more profound if we in our research step outside the diagnostic imaging which, for instance, made their entry on the US market during the so-called Pre-Amendment era (before the Medical Device Amendments which took effect in 1976). Also, regulatory environment has changed dramatically since that time, both in the US and Europe, as the findings of several sources suggest (Makower J., Meer A., Denend L., 2010; PwC 2011; Donawa M., 2010).

Therefore, the present study is dedicated to expanding the knowledge about this particular element of the sectoral innovation system. It is focused on the regulations of approval in medical technology industry in the United States and European Union with regards to how different frameworks influence the industrial leadership and views the industry in broad terms. The sections below present the theoretical foundations for the study.

### 3.2 Institutions, technologies and industrial performance

Previous discussion highlights the role of institutions as one the key building blocks of sectoral innovation system together with knowledge, technologies, actors and networks. Douglas C. North in his work “Institutions, Institutional Change and Economic Performance” (1990) suggests accordingly, though in more general terms, that institutions, which are defined as “humanly devised constraints that shape human interaction” (North D., 1990, p.3) together with technology define the “transaction costs of human interaction”, and, therefore, influence directly the performance of economies.

This view is based on theoretical approaches in evolutionary and institutional economics that emerged in attempt to fill the gap between the conventional neoclassical theory which addresses the “ideal” markets and abundant empirical evidence that suggests its various imperfections. In particular, traditional theory has economic equilibrium as its outgoing point, where optimal resource allocation is achieved (Nelson R., 1994). It is also assumed that the objective of maximizing individual wealth solely determines ones choices, which, in their turn, are absolutely efficient, i.e. the actors possess the perfect information about available alternatives, can adequately assess them and are able to act upon them. The reality shows, however, that human interaction involves a good deal of uncertainty, as information and ability of an individual to process it are limited. Human behavior is not either limited to just the wealth-maximizing one (North D., 1990). Imperfections are expressed in transaction costs of human interaction that arise in connection to the need of getting better information and better understanding of what it implies. Here, institutions work as a “transmission belt” for “preserving knowledge” or, a tool for making sense of reality (Hodgson G., 1998, p. 180).
The transaction may be more or less costly. Importantly, the more costly the transaction is, the higher impact the institutions have on economic performance. How adequately are the institutions in resolving the transaction costs depend on the complexity of the environment and also motivation (utility of the information for the agents) and ability of agents to measure and enforce the environment (North D., 1990).

Wide range of institutions (infrastructure, regulations) is shown to be co-evolving with technology (Nelson R., 1994). Rich body of research suggest that technology evolves along certain trajectories (Abernathy W., Utterback J., 1978) and may be subject to increasing returns rule (Arthur B., 1990), which makes the industry and respective technology get caught in a certain path, not necessarily the optimal one. As technologies evolve as a complex whole hand in hand with the supporting industry structure and institutions, just the same rule of positive feedback influence the institutional change as well, with the difference that it is a more complex process determined by interactions of political and economical factors, various actors with different bargaining power, “cultural inheritance”, which influences the change through informal constraints (North D., 1990, p.104). Accordingly, the institution’s evolution is path dependent, which means that the resulting institutions are not necessarily effective.

Growth and effectiveness of the industry depend on how rapidly and effectively a support structure grows up. Institutions tend to adapt and change (with some lag) in response to signals from developing industry (Nelson R., 1994). Then, if the industry undergoes that technological shift, institutions often fall behind the technological development. Furthermore, the objective of effective technologies’ development explicitly requires a nation to create a set of institutions supportive of these technologies and in some cases institutional reform may be required (Ibid).

### 3.3 Government regulation as an institution: rationales and theoretical tradition

Government regulation of markets is an institution which is shaping industries through setting official rules of the game for business (Balleisen E., Moss D., 2010). Theoretical foundations for regulation, as one can see, is consistent with that for institutions in general, described in the previous section, though applied to the special arena, namely: relations and balance between governments and markets.

The main rationale for regulation is mitigation of the market failure (Ibid). Explanations of this rationale, just like those for institutions in general, are based on deficiencies of conventional theories which assume the markets as being self-efficient, guided by so-called “invisible hand”, i.e. self-interest which is making an individual provide what the other society members require at the lowest price, thus, maximizing the well-being of the whole society. In reality such an ideal picture does not exist and markets often produce a failure: information imperfections, externalities and unfair competition which require intervention from outside the market to be cured (Stiglitz J., 2010).

As market failure emerges as a side effect of market exchange, its cost is not obvious for any given individual and the attempt to solve it from inside the market would mean bargaining everyone with everyone. This is hardly achievable due to immense transaction costs. That is why government which logically undertakes to represent the society in negotiations with business, thus, providing savings on transaction (Ibid). Similarly, with regards to harm caused as a result of market failure, regulation is preferable to, say, class actions, as it mitigates inappropriate behavior in advance, setting boundaries on actors,
rather than curing consequences when the harm is already caused. Finally, compared to other ways of governmental intervention, such as taxation, regulation is more flexible as it imposes non-linear effect and includes input tools (e.g. standards) together with output ones (fines) (Ibid).

Regulation is evolving with time and economic knowledge is an important driver of this evolution. Governments refer to this knowledge coming from professional sphere, practical knowledge and cultural beliefs and values to legitimate its policies (Furner M., Supple B., 1990). Here, if the knowledge required is specific and complex, then mediating institutions may be required in order to facilitate the dialog of government with industry and public. Such institutions emerge in form of specialized agencies, able to provide both the state and the public with expert opinion (Ibid). Furthermore, if regulatory process requires so, legislative functions may be also delegated to an expert agency, otherwise government takes a risk to fall out of context and fail to address current market issues (Stiglitz J., 2010).

Obviously regulation is not always effective which can occur either due to incompetence or corruption or bounded rationality of the regulator (Ibid). However, scholars traditionally tend to departure from George Stigler's theory of regulatory capture (Balleisen E., Moss D., 2010, Carpenter D., 2010, Wittman D., 2010) which implies that regulation promote the interests of those stakeholders which possess more bargaining power, and, hence, one can define who lobbied one or another decisions by finding out whose interests the regulation serves the best. However, one should take his argumentation cautiously, as no solid evidence of this connection exists (Wittman D., 2010). First, different stakeholder groups may be equally unsatisfied with a policy, which makes them subjectively point to each other, as if the policy would be the result of counterpart group's pressure. Second, if different policies have been adopted on the same issue in, say, two different cities, it may be due to objective reasons, rather than due to different ability of interest groups to influence decisions in each of these cities. Competition among regulators should exist as well, which works against capture, so one can say that regulations should be regarded as “innocent until proven guilty” rather than other way around (Ibid, p.210).

Also, for the sake of this study, it should be appropriate to mention that inefficiency of regulation is not always a consequence of the policies design; it can arise from their inadequate implementation (Stiglitz J., 2010).

### 3.4 Approval regulations: a tool for creation of markets

In general though, regulation produces broader spectrum of effects on the industry than simply addressing market failure. It sets the appropriate balance and optimal relationship between market and state, economy and polity, individual and society (M. Furner), benefits and risks, help resolving possible ethical conflicts (Francis J., 1993). One can say that regulation is an “integral part of broader social system that encompasses economic institutions and relationship” (Balleisen E., Moss D., 2010, p. 4). Approval regulations represent a good example on how deep and multifaceted may be the effects of regulation on markets.

Different markets are characterized by different grades of information failure severity. Such markets as pharmaceuticals or medical technology are subject to serious information distribution and learning constraints, due to both high complexity and asymmetry of information (Carpenter D., 2010). Namely, consumers on such markets, if left to decide the
matter for themselves, are not able to assess real quality of products, so they tend to choose worse and cheaper ones, pushing higher-quality products out of the market.

To protect the consumers from inadequate products approval regulations are in place. Approval regulations imply that manufacturers are granted by the state with rights for production and distribution of their products in return for presenting enough evidence of safety and effectiveness, which very often assumes testing of the product during the submission procedure (Ibid).

Such regulations, therefore, establish confidence in consumption, and, importantly, prompt manufacturers to provide larger amounts and better quality information than they would give out otherwise. This requirement, in its turn, creates the incentive for manufacturers to invest more in R&D and undertake higher-level scientific investigations, which leads to completely different structure of demand on these markets and creation a marketplace for better products. In other words, regulation in this case provides the very possibility to exist for the markets superior with regards to quality and information, and very different from those markets that would have existed without these regulations. Surprisingly, even sales on such markets are shown to rise after adequate amendments in regulations taking place (Ibid).

Additionally, approval regulations contribute to fairness in actors’ behavior, as higher requirements to information disclosure imposes constraints over possible pressure of interest groups and fraud (Ibid).

### 3.5 Regional dimension of regulation: US and EU

As mentioned before, institutional development and change depend on history and evolution, and therefore, it should vary from region to region and study of similarities and differences of the same policies in different countries may give an input for better understanding of relations between market and state.

Mary O. Furner and Barry Supple compared patterns of relations between “political institutions, economic change and economic knowledge” (Furner M., Supple B., 1990, p.3) in the United States and Great Britain as two countries which are similar with regards to their political and economical traditions, but different in cultural and institutional terms. Their study showed that previous evolution shaped differently by the cultures and traditions and specific challenges each of these countries faced, influences industrial settings and competition patterns as well as to what degree the institutions in each of these countries are flexible and to what degree they may change. Namely, the US is characterized by dualism in ideas and cyclical evolution of institutions as well as shorter periods any given policy is a mainstream, compared to more consistent institutions in Britain (Furner M., Supple B., 1990).

The look into the history, thus, gives a possibility to formulate the factors forming the regulatory traditions, which include: theoretical developments in relevant knowledge base; practical knowledge and views and beliefs prevailing in the society), previous path of regulations’ development, cultural and institutional settings (Furner M., Supple B. 1990; Furner M., 2010).

For the sake of this study, therefore, it should be appropriate to take into account the history of regulation in the US and European Union. Neil Fligstein (2010) traced these two systems beginning from the Treaty of Rome (1957) which laid grounds for the EU and
analyzed how this evolution contributed to formation of dominant regulatory strategies in both regions.

The development of European Union was driven by the goal to create a single market on the territory of all member states. The process of merge logically involved “negative integration”, i.e. removing barriers to trade, which lead to several impasse points, as member states feared the dangers of such a measure, answering with protectionist policies. However, the oil shock of late 1970s prompted member states to find the way out of the crisis which served as incentive for them to figure out the necessary conditions of continued integration. Pre-requisite for success and working alternative to protectionism found to be “positive integration”, i.e. establishing on the whole territory of European Union guarantees of protection of all the interested parties (e.g. adoption of proper employment policies, other social protection means such as environment and product safety policies). In the end, as one can see, the combination of both positive and negative integration projects indeed lead to creation of single European market, although a great deal of autonomy in various regulatory issues of single member states is preserved (Fligstein N., 2010).

Oil shock affected the United States as well, which came up with different solution for the same problem, namely deregulation, which included loosening control over certain industries and antitrust policies, which gave advantage to big corporations on the international arena, etc, i.e. measures were mostly limited to negative integration specialty. The author argues that the economic growth in the US actually suffered. Moreover, the most profitable industries in the US, such as telecommunication and biotechnology are those where positive integration is adopted. This suggests that deregulation alone is harmful for industries, if applied without positive integration (Ibid).
4 Basics of medical device regulations in the US and EU: overview and comparison

4.1 Schemes of US and EU regulatory systems and responsibilities of the actors involved in them

Regulation of medical devices in the US is in full responsibility of Federal Government (Makower J., Meer A., Denend L., 2010, Phillips P., Kessler L., 2010, Davis S., Gilbertson E., Goodall S., 2011). The regulatory system is organized in a centralized way and the key actor in it is the Food and Drug Administration (FDA 2011-2). This agency’s main responsibility is to protect the American people’s health by “assuring safety and effectiveness” of different types medicinal, food and cosmetics products, including medical devices. FDA coordinates the medical device approval system which results in permission for the device to be marketed in the US; it is also in charge for keeping track over devices already on the market and applying enforcement measures to manufacturers if required.

In contrast to the American system the responsibility for the medical device approval in the EU is shared between several actors both on the all-European level as well as on the member state level. See the fig. 1 for brief schemes of US and EU regulatory systems.

All-European legislation concerning medical devices is produced by European Commission, the EU’s executive body responsible for development of laws and governing all-European policies and funds (European Commission, 2011). Further, each of now 27 EU member states has its own Competent Authority which functions are similar to those of FDA in implementing the corresponding laws, supervision over clinical trials, ensuring compliance and enforcement, providing post-market surveillance (Jefferys D., 2010).

However, unlike FDA which undertakes the whole range of corresponding functions, including pre-market reviews alone, Competent Authorities of member states subcontract so-called Notified Bodies which perform the certification of goods on the member state’s behalf. Although accredited by the Competent Authority of a member state, Notified Bodies are free-standing privately-held for-profit organizations. There are 72 Notified Bodies in the EU authorized to perform the approval process for medical devices (Davis S., Gilbertson E., Goodall S., 2011). In other words, in contrast with the US approach, manufacturers are not obliged to undergo governmental review in order to get access to the market in Europe (Shuren J., 2011).

Furthermore, there are dissimilarities in underlying principles of responsibility allocation assumed by US and EU regulations. In the US a manufacturer in order to comply with the law must prove both the device’s safety and effectiveness, while in Europe it has been enough to demonstrate safety and performance according to the criteria assigned by the manufacturer (Shuren J., 2011, Allina A., 2010).

At first glance these requirements are similar. However there is a profound difference: in US case, the responsibility to assess effectiveness, i.e. the measure of how well a device is addressing some medical problem has been in the hands of government and in the EU case this responsibility has been in hands of medical practitioners. In other words, in the US model the balance between state and public responsibility is shifted towards the state’s side while EU has given away the issue to the professional society to manage.
Fig. 1. Brief schemes of US and EU regulatory systems. Upstream links are not shown
This responsibility allocation is debated intensely (Dickinson J., 1997). Proponents of governmental responsibility suggest that the benefit to the patient should not be the market issue in order to prevent speculations and fraud (Allina A., 2010). On the other hand, its opponents suggest that government does not have enough resources and competence to always make correct decisions on effectiveness and in the US it leads to delays in device reviews and subsequent delays in providing patients with state-of-the-art technology.

4.2 Clearance/approval process and its stages: comparison of US and EU approaches

Regulations are applied to the product during all its life span (Cheng M., 2003, Feigal D., 2010) and therefore address each of the product’s life cycle stages specifically. In relation to the product life cycle there are two main stages of regulatory process (see fig. 2) (Feigal D., 2010): pre-market and post-market stages, forming the corresponding regulatory cycle (Ibid). Below, the US and EU approaches will be compared for each of the two regulatory cycle stages.

### Fig. 2. Medical device product life cycle and relevant stages of the regulatory process

#### 4.2.1 Pre-market stage

As the goal of the regulatory review on the pre-market stage is to ensure user protection and safety, the “regulatory philosophy” related to medical devices proceeds from the magnitude of risk which a medical device’s use may mean to the public safety (Powers D., 2006). Safety cannot be absolute, in other words, there is always a certain, nonzero probability of risk that can be related to the device’s use. Therefore regulations address the safety issue in relative terms: safety represents a relation of residual risks and overall benefits (Cheng M., 2003, Powers D., 2006).

The concept of risk is a critical element of both US and EU regulations. Natural logic suggests that the devices that pose greater risk should be regulated in a more stringent way than the lower-risk ones. This assumption in its turn leads to the need for risk-based classification of devices and this classification helps to illustrate one of important historically formed differences in regulatory approaches in the US and EU.

In the US two-dimensional classification of medical devices is adopted, which estimates both risk and similarity to pre-approved devices. FDA divides medical devices into three
classes according to risk (Phillips P., Kessler L., 2010), meaning that the approval procedure’s scrutiny level should rise proportionally to risk class of the device. In practical terms it means that devices of higher risk classes are subject to greater number of general and special controls (such as labeling, post market surveillance etc.).

Similarity dimension is a base for one of the two distinct procedures of market approval. Simpler and more lenient pathway is called Pre Market Notification or 510(k), and is intended for products which proved to be similar to another one already on the market. Similarity here is defined basing on the device’s intended use and technological features which both should be the same as those of the analogous marketed device, or, in the case if its technological characteristics appear to be different, the device should not call for new questions concerning safety and effectiveness (Phillips P., Kessler L., 2010). The other pathway, assuming thorough pre-market examination, including clinical studies, called Pre Market Approval (PMA) is used for products based on completely new approaches/technologies (Ibid).

The low-risk device of Class I do not normally require 510(k) notification, moderate-risk Class II devices are usually subject to 510 (k) and high-risk Class III devices are subject to PMA path (Phillips P., Kessler L., 2010). However, as one can see, this classification spawns confusion, as risk itself is not connected in any direct way to similarity. For instance, should a low-risk device, though based on completely new technology still be forced to go through PMA? Addressing these issues, some roundabout ways are created, such as de novo 510(k), applied for the cases like one specified above.

Anyway, risk consideration alone does not indicate which of the two paths the device will hit and the decision how heavy the device will be regulated depends primarily on the principle of its similarity to any predicate device. In practice, the classification adopted at FDA is descriptive. Similarity is considered first: a device seeking 510(k) is classified into one of 16 large panel groups (cardiovascular, anesthesiology, etc.) (FDA 2011-3) and then further into more specific types. The risk class a device is assigned afterwards, on the base of each particular device type (Cheng M., 2003), while, starting with similarity classification, as a matter of fact, the agency considers not three but about 1800 device classes (Phillips P., Kessler L., 2010).

In Europe the classification is a pure risk-based one (Cheng M., 2003). Class I is applied to devices which are self-regulated by a manufacturer (with probable occasional audits of Competent Authority representatives), Class IIa is subject to partial quality system review, Class IIb requires full-blown quality system and partial review of design and Class III - full-blown design dossier review (see the fig. 3).

After the risk class is assigned to a device, appropriate level of regulatory control is applied to it in order to ensure that risks are as low as possible and benefits are as high as possible (Cheng M., 2003) and it should be made sure before device reaches the market. On the stage of pre-market review two basic elements of the product safety are in the focus of both US and EU medical device regulations: the product is assessed from the perspective of technological safety (system failures) as well as safety in use (human errors) (Ibid).
4.2.2 Post-market stage

Practice suggests that it is not possible to predict all types of possible adverse events during pre-market risk assessment (Cheng M., 2003). It is of vital importance, therefore, to provide surveillance over devices while they are on the market.

There are two ways to collect the information of the devices in use: post-marketing studies and adverse event reporting (vigilance) (Cheng M., 2003). Post-marketing studies may be required as a special control within 510 (k) or PMA paths or specifically claimed in case of serious device-related event that was not foreseen in advance. Adverse event reporting is mandatory both in US and EU and means that a manufacturer or user should inform authorities about serious incidents related to device use.

The main difference between the US and an EU system of post-market records is the way to process this information rather than collect it. In the US the register where information about adverse events is accumulated is an open-access source (Makower J., Meer A., Denend L., 2010), on the contrary there is no all-EU certificate recall register either (Donawa M., 2010) as well as no centralized authority gathering and publishing the post-market records (Shuren J., 2011). The Notified Bodies do not report to Competent Authorities case by case, moreover, the case information is deemed confidential (Shuren J., 2011).
The reason why there is no centralized surveillance system in Europe is simply that it has not been arranged yet and this is a space for improvement for EU regulations. The openness of the US register of device reporting has been criticized as the sensitive data end up in possession of all the interested parties, even those without direct responsibility for acting upon it (Dickinson J., 1997).

### 4.2.3 Regulation of processes: quality system

Regulation of processes helps to ensure the overall consistency of quality achieved in each aspect of company’s activities and in manufacture in particular. It is implemented via establishing “generic management standards” or so-called quality management system standards (Cheng M., 2003).

The goal of quality system illustrates a proactive approach to management of quality where the process failures are prevented in advance by establishing a special mechanism for this purpose in contrast with reactive approach where failures are reacted upon after they have happened. Quality system embraces all the stages of the regulatory life cycle although the adoption of it is included into pre-market stage requirements.

In the EU the applicable standard is ISO 13485:2003 that has the core requirement set equal to ISO 9001 series supplemented by special legal requirements for medical devices. The quality management system requirements of FDA are called Quality System Regulations (QSR) and are found in paragraph 820 of Code of Federal Regulations (21 CFR 820). The two systems are very similar, apart from some a bit more stringent requirements of QSR regarding process validation and keeping quality records (Donawa M., 2009). In general, both systems are advised to be applied simultaneously keeping in mind implementing maximum of both.

### 4.3 Legal framework for medical device regulations in the US and EU

The schemes shown on the fig.4 illustrate how the legislation covering medical device regulation in the US and EU works (Jefferys D., 2010; Hutt P., 2010; Hanna M., 2009-1; Hanna M., 2009-2).

In the European Union, the three EU Directives covering medical devices are the following: Active Implantable Medical Device Directive 90/385/EEC, Medical Devices Directive 93/42/EEC and In Vitro Diagnostic Directive 98/79/EC (Jefferys D., 2010). The Directives are applied in the whole EU and built into laws of each member state, all of them are mandatory.

The compliance with the essential requirements given in Directives is supported by various harmonized standards which provide more detailed guidelines for manufacturers on how to approach one or another issue (Jefferys D., 2010, Cheng M., 2003). For instance, compliance of the risk management process of the manufacturer to the standard ISO 14971:2007 automatically means compliance to essential requirements of Medical Device Directive applied to risk management of medical devices (Powers D., 2006). More specifically, standards are “documented agreements” containing detailed criteria to ensure that a product, process or material meets certain performance goals (Cheng M., 2003, p.18).
Use of standards as a part of regulatory regime has several advantages to respective governments (Cheng M., 2003):

- **Standards help governments save resources**: they are developed by professionals in the area without involvement of governmental resources. On the contrary, resources pooled in the industry and professional communities (which are greater than those governments possess) are involved.
- **They facilitate trade across borders** by establishing the common language of requirements among different nations and, subsequently, contribute to increase of welfare and quality of life overall.
- **They address technological development effectively**, because, unlike laws can easily be updated and changed according to current technological advancements.

Moreover, the standards applied on the company level ensure the general approach that the manufacturer applies to its processes is appropriate, which means that conformity to the standards proved once for a product will be applicable to the other products of this company as well (Donawa M., 2010).

FDA issues its own guidelines on how to address the laws, however, in the end it is up to a reviewer to decide what information a manufacturer should provide on each certain case (Phillips P., Kessler L., 2010). FDA also recognizes a series of consensus standards, such as some of ISO standards, as an evidence of compliance to American law (Ibid). Some attempts are taken in the US to make the regulatory approval process easier for those manufacturers who are certified in accordance to these standards. However, it seems that the process of clearance/approval in general is still dependent on FDA’s guidelines and
reviewer’s oversight more than on the external standards (Jefferys D., 2010). Usually FDA reviews each company product separately (Donawa M., 2010).

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As to conclude the current chapter, it can be pointed out that the American and European regulations of medical devices are based on similar regulatory reasoning to ensure public safety. However, the differences, of both technical and deeper “philosophical” nature, are also apparent.

The concentration of all resources, responsibilities and roles in regulatory process at FDA in the US is contrasting with more diversified structure of relations between several different actors in the EU. It can be observed equally with regards to allocation of responsibilities for pre-market review between government and private bodies, as well as on the level of letting professional medical community decide the device effectiveness issue.

Projection of the same situation one can see in both American and European legal frameworks. Although both American and European laws are not very detailed, they are supported with more elaborated requirements: standards in EU case and guidelines in US case. FDA prepares guidelines on its own, while the standards are prepared by free-standing international organizations, possessing greater possibilities to recruit competence than government of any single country could afford.

Furthermore, the role of reviewer in American context is much more prominent, as he/she is granted with the authority to say a final word in law interpretation, compared to more “technical” role of the European reviewers. The American classification of medical devices as a base for regulatory scrutiny seems also to emphasize the role of reviewer which requires the set of controls to be presented by a manufacturer on a case-by-case basis.

Finally, records on pre-market inspections and medical devices safety are gathered in a centralized way in the US and can be accessed by public, although on a scale of the E.U. there is no common register of the kind and most part of information on reviews and certification is deemed confidential.

Overall, except the arrangement of post-market surveillance and vigilance records, European approach seems to be more efficient, i.e. more standardized and, therefore, possessing higher capacity to process the industry inquiries compared to American one.
5 Causes and direction of change of medical device regulations in the US and EU

5.1 Evolutionary paths of regulatory policy development

5.1.1 US and EU regulation of health care: history background and trends

Health care both in US and EU went through a serious transformation in the middle of twentieth century, namely during the decades after the Second World War (Francis J., 1993). During earlier years technological innovation did not cost too much to the state, at the same time, bringing considerable improvements into health care. As an example, the introducing of drinking water standards had a profound effect on success in infectious disease prevention and control. As the technological advancement accelerated, however, in the second half of the century, technologies got more and more expensive. The health care performance increased, but the expectations of the society increased in the same pace with this progress. Thus, the perceived benefits became less and less prominent on the background of quickly rising costs. The trend is emphasized by demographic changes: the biggest portion of health care expenditures is consumed by elderly people and this figure rises in time as the population is ageing (Ibid).

The central issue that arose as a result of this trend is how to provide access to care to as many people as possible at the lowest possible cost. As a consequence, the regulations leave less and less autonomy in making decisions regarding choosing therapies to health care professionals assigning this responsibility namely to the stakeholder that is paying for the healthcare in a given country (Francis J., 1993). The equilibrium: government vs. public shifts towards greater influence of government.

Also, the pressure over the industry (manufacturers) is increasing, as in the situation of cost constraints the quality control issue becomes of prime importance and pre-market control of health care products gets more and more stringent.

5.1.2 History and evolution of medical device regulations

Medical device regulations are affected by both general trends discussed above as well as issues related to particularities of medical devices as a specific product group. In the beginning of the twentieth century pharmaceuticals, not medical devices were the main focus of government regulations (Hanna M., 2009-1). Pharmaceuticals were many in number and their effect on healthcare was considerable. Medical devices, on the contrary, were few, not very effective, in most cases harmless and viewed by official medicine as a little bit of healer's kind of tools. During two decades after the Second World War medical technology developed quicker than ever before bringing problems and risks connected to growing use of medical devices. Governments in both Europe and the United States faced the demand for establishing an appropriate regulatory framework which would guarantee the public safety, yet, an access of the public to contemporary technologies (Ibid).
5.1.2.1 US medical device regulations’ evolution

In US Federal Food, Drug and Cosmetics Act of 1938 (usually called simply as “the Act”) medical devices were merely mentioned. Subsequently, the first attempts to regulate medical devices added up to classifying them as a separate group under pharmaceuticals and applying to them the approval model used for drugs. However, several serious incidents related to devices’ use, some of them deadly, indicated this approach to be ineffective, which called for special legislation for medical devices and lead to adoption of Medical Device Amendments to the Act (MDA) in 1976. MDA for the first time demanded the pre-market approval for medical devices and are recognized as the origin and base of modern US medical device regulation (Hanna M., 2009-1; Hutt P., 2010).

MDA assigned FDA, an agency within the US Department of Health and Human Services, which was then in charge for pre-market regulation of drugs in the US, to be responsible for approval of medical devices as well (Hanna M., 2009-1), more specifically its division called Center for Devices and Radiological Health (CDRH) (FDA, 2011-4). Thus, the government through FDA was granted authority to interpret legislation and create the guidelines for manufacturers on how to address it, review and inspect, process recalls and enforce the law.

In connection to the adoption of Medical Device Amendments in 1976 and introduction of pre-market review of devices the question also arose: what to do to the devices already on the market (which were quite many by 1976)? Answering the second question, FDA let all “pre-amendment” devices stay on the market (Hanna M., 2009-1). But then, the next question followed: what to do with the devices developed after 1976, but similar to those already approved? Meaning that the device should not undergo the whole approval process if it is substantially equivalent to the marketed device (“predicate device”). FDA came up with two distinct regulatory pathways discussed above, i.e. 510(k) (named so after the corresponding clause in MDA) and Pre Market Approval (PMA) (Phillips P., Kessler L., 2010; Hanna M., 2009-1).

Further amendments were introduced in 1990 in the form of Safe Medical Devices Act, making the regulations stricter. If previously the 510(k) notification was a pure formality and 510(k) applications did not go through the scientific review, after 1990 the “notification” actually transformed to “clearance” and now FDA took time to review all the incoming submissions. After 1990 the speed of application processing by FDA slowed down dramatically (Hanna M., 2009-1). FDA realized that to perform better the agency needs more people and to provide these people with more training, which lead to vast increase in application fees (Hanna M., 2009-2).

To ease the excessive pressure on manufacturers, with FDA Modernization Act of 1997, simplified versions of 510(k) were developed for some particular cases: “Special”, “De-novo” and “Abbreviated 510(k)” (Hanna M., 2009-2). So-called Least Burdensome Means standard was adopted at FDA, saying that FDA reviewers should limit their requests to the most relevant information so that the review is organized in the least burdensome way. This amendment was thought to be the most appealing to the industry, however in practice it is not implemented to full extent (Ibid).

Nowadays FDA makes attempts to adopt electronic submissions, replacing paper ones, which would help to organize the interaction of the agency with the industry in a more structured and reliable way (Ibid). Some efforts are made to streamline the low-risk
devices reviews and make the regulatory procedures more transparent and predictable (Shuren J., 2011). It is the upcoming years that will show the results of these efforts.

5.1.2.2 European medical device regulations’ evolution

The current European regulatory system is much younger than the American one. The Directives addressing Europe as a single medical device market were created during 1990s and became mandatory even later, the last one as late as in 2003. Before that time European regulation was represented by a variety of approaches: each member state had its own system, all of them were different from each other (Donawa M., 2010). Moreover, during 1980s regulation within each country developed quickly with the risk to diverge even more in the future. This was a very alerting sign for the industry as it meant growing barriers to trade while the industry was interested in consolidation of Europe into a single market (Suppo M., 2003; Donawa M., 2010). European regulators were also very aware of the US method that was recognized as a gold standard during that time. Attempts were even taken by some EU member states to adopt similar system on their territory. However, supposedly due to the efforts of many different stakeholders, primarily the industry, European legislation went another way and created a system which was significantly distinct from the American one (Donawa M., 2010).

The harmonized method proposed by the European Council in 1985 was named “The New Approach” (Jefferys D., 2010, Donawa M., 2010) as it contrasted in an important way with earlier less successful attempts to harmonize regulations among the member states: Old Directives contained thoroughly elaborated technical guidelines, so, it took time to develop and adopt them. Furthermore, by the time they got adopted they were no longer topical. Therefore the advantage of The New Approach Directives is that they contain the generic demands only, called essential requirements, which then are supported by more detailed guidelines given in various applicable standards proposed by European standards organizations, not by the European Commission.

Recent revision of the Directives in 2007 addressed the information exchange deficiency throughout European Union, by demanding the all-European information database to begin working by September 2012. It introduced also some means to help establish the common vigilance system in Europe (Donawa M., 2010).

However, these amendments provoked discussions within the industry as some changes introduced make the approval process more complicated. Some experts expressed fears that these amendments indicate the negative trend moving EU regulations from the liberal path (Veed R., 2010). Next revision of the Directives is expected in a few years from now, in 2015 (Donawa M., 2010).

5.2 Specific national/regional patterns of interactions of the society and the state

According to the study by M. O. Furner and B. Supple (1990), discussing the interactions of the state, institutions and ideas in Great Britain and United States, the British state possess government which is overall less open and hard to access from the society side than that in the US. Policy-makers in Britain represent homogeneous groups, majority of them traditionally coming from similar educational background, ideas and policies follow rather consistent and uniform pattern through time.
While continental Europe is different from Great Britain in many ways, these countries demonstrate yet greater power of state with the public having more abstract view on it compared to “operational” attitude to governments of the society in Anglo-American context (Furner M, Supple B., 1990). Authorities on the level of European Union represent yet higher level of abstraction.

In the US diverse forces have easier access to government, which itself has less homogenous representation. Different branches and institutions forming the state are very often held by opposing social groups. This makes the whole system subject to tensions and cyclic recurrence of ideas and policies, which is often referred to as “political pendulum” swinging between left and right extremes. Another consequence of this pattern is limited capacity of state to sustain any particular course, therefore the agencies with “quasi-legal” authority, more closed and opaque compared to government, emerge to enable more consistent path of society development (Furner M, Supple B., 1990), with FDA being the textbook example.

5.3 Theoretical developments in relevant professional knowledge, practical knowledge, beliefs and values prevalent in the society

Democratic state requires “knowledge base adequate for making and defending policy decisions” in order to be able to perform consistently (M. Furner, B Supple, p.10). This knowledge may come from both interested actors, in the form of more practical knowledge possessed by industry or attitude of the society, as well as from the professional arena, producing more abstract theories.

The approval regulations are based on the same philosophical foundations republican traditions overall dwell upon (Carpenter D., 2010) and illustrate public awareness of the dangers which unregulated market of the kind bears. US and EU have a lot in common what concerns basics of these two democracies (Furner M, Supple B., 1990).

However, it appears that apart from this background the actual theoretical base for legitimating of this or the other policy is either limited or not used to a full extent (supposedly both). In this situation more specific foundations of everyday regulatory decisions come from the current political climate, culture, society views and opinions (Phillips P., 2008).

This assumption is indirectly supported by the fact that FDA culture became closed and opaque with regards to what is going on inside it, and consequently, risk averse and avoiding making decisions as a result of the pressure on the US regulatory system from different actors, sometimes with opposing interests. Some observers also point out pendulum-like movements of FDA attitude between “risk-tolerant and risk-averse regulatory oversight” (Makower J., Meer A., Denend L., 2010, p. 33), however, the general trend is towards avoiding risks. Although some research exists that is able to neutralize at least a part of the society claims (such as reports on very low recall rates in the US, which could be used as an evidence of enough scrutiny imposed by FDA on manufacturers), FDA does not always take advantage of such data (Makower J., Meer A., Denend L., 2010).

If more knowledge had been available and existing theoretical foundations had been used more actively, the trend described would have likely been less apparent. This altogether

As the responsibilities and liabilities connected to regulatory process are shared among several actors in the EU, European authorities seem to need to legitimate their decisions mainly when legislation is created or amended. On these occasions stakeholders of regulations are called to share their opinion and expectations on the discussed documents (Donawa M., 2010; European Commission, Consumer Affairs, 2011). This mechanism proved to be democratic, e.g. even the IVD directive first draft was prepared by the industry (Suppo M., 2003). The approval process is based on applicable standards, which are also a joint creation of different stakeholders.

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As one can see regulatory system in the US is mature. Issues such as classification of devices and the role of FDA as a key player in it are historically formed. Moreover, on the general background of information transparency and in American society FDA has developed a sort of immunity to the pressure from society. It is inert to changes induced outside the agency, and it seems as even if some changes were announced, it would not be easy to actually adjust the FDA-giant to the new situation. Moreover, political uncertainty, resulting in pendulum-like movements of the society in general, makes it complicated to introduce changes in any particular direction consistently.

EU system has been created very recently and from the very beginning the New Approach has addressed the problem of regulating such a diverse market as medical devices in a timely manner. The system seems to have a capacity to adjust incrementally, which also agrees with general European ability of being consistent to the course once chosen.

As for the knowledge base for legitimating of policies, it is apparent that FDA and European officials each need such a base to a different degree. If in the EU such legitimacy is required to be supported on occasion, FDA seems to need it constantly to balance the stakeholders’ interests effectively.
6 Performance of American and European regulatory systems

6.1 Stakeholders of regulations, their relative motivation and ability to measure and reinforce the desired path of regulation’s evolution

Among stakeholders of medical device regulations the following actors can be mentioned: the industry, venture capitalists, public, news media, health care providers, insurance providers (Makower J., Meer A., Denend L., 2010; Dickinson J., 2009) as well as legislators and regulators: US Congress and FDA in case of the US and European Commission, Competent Authorities of Member States and Notified Bodies in case of the EU (Cheng M., 2003, Jefferys D., 2010). Although similar stakeholder groups present both in the American as well as European context, their relative motivation and abilities to influence the regulatory policies on each of these markets are different.

As mentioned before, the voices of different stakeholders in the US are more articulated compared to Europe. Also, in the US a centralized approach to gathering health care statistics is applied, in contrast to the union of independent countries. As a consequence, FDA and its policy have been exposed to intense attention and criticism (Makower J., Meer A., Denend L., 2010) from various stakeholders (Dickinson J., 2009). The interests of these stakeholders are often opposite. Media and public mount an attack on the industry, which in turn wants to be left alone to be able to work, health insurance does not want to pay for device failures, patients affected by defective devices want the opposite, and FDA under pressure wants to keep the status quo (ibid).

This does not mean that stakeholders of European regulations have no power to influence the policies and important decisions such as creation and amendments of Directives are appropriated by officials alone. In fact, the dialog between different society groups is initiated by the European Commission on such occasions (European Commission, Consumer Affairs, 2011; Donawa M., 2010).

The same public consultations are held in the US as well (consider, e.g., the Workshop on effectiveness of 510 (k) arranged by Institute of Medicine, 2010, the present study references several speeches within this workshop). However, the point is that the attention to the regulatory process and influence of different society groups there is more apparent and concentrated than in EU.

6.2 Evolution of environment complexity

Complexity of the environment can be viewed through the prism of costs which the actors in the industry bear to get the information required for making adequate choices (North D., 1990).

As a specific scientific and technological field, medtech is represented by diverse range of technological applications; however one can say that it is characterized by rather complex products involving a number of different technologies coming from different branches of science. Furthermore, medical technology product usually is a complex system that consists of several different modules (such as interface, drug delivery or physical action units, measurement unit, etc.), each of which can be a complex of several technologies (Hiderfjäll, P., 2010). Quite often opportunities come from other sectors as well, e.g., communication technologies.
The technological complexity of the industry is a cause of serious learning problem in the sector, as actors, without proper tools of understanding the medical technology are unable to define effectively the risks and benefits of medtech products (Carpenter D., 2010), and, consequently, seek for indirect ways of assessing what is good or bad for them, tracing headlines, or someone else’s informal interpretations (Makower J., Meer A., Denend L., 2010).

Various sources (Makower J., Meer A., Denend L., 2010; Gollaher D., Goodall S. 2011; PwC & BIOCOM, 2010; Carpenter D., 2010; Shuren J., 2011) agree that the technological advancement in the field has been accelerating in medical technology during the recent years. Moreover, now the devices which claim to be substantially equivalent to those already sold are getting more and more distinct from their approved analogs compared to what one could observe before (Phillips P., Kessler L., 2010). Such rapid development of technologies demand superior technical expertise even from regulatory agencies, which require superior resources to be spend by regulators to attract the appropriate competence (Makower J., Meer A., Denend L., 2010, Shuren J., 2011).

The pressure of technological advancement on FDA is immense, especially keeping in mind resource constraints that the agency is suffering at the moment (Shuren J., 2011). European authorities, although less dependent on resources and inside competence, also express concerns about keeping in terms with rising technological demands (European Commission Consumer Affairs, 2011).

6.3 Output performance of the US and EU regulatory frameworks
In the following section the output performance of the US and EU regulatory frameworks are discussed. With regards to medical device pre-market approval the effectiveness can be defined as a sum of efficiency and ability to perform the main goal of regulation: ensuring public safety.

6.3.1 Output efficiency of the US and EU regulatory systems
Perceived performance of American and European systems regarding time, cost and overall impression of companies that got their products through both American and European approvals has been determined recently in two surveys of industry executives. One of them is a study of views of 200 companies on pre-market approval conducted on the base of Stanford University, supported by industry and venture capital associations MDMA and NVCA in the US and the consulting agency PricewaterhouseCoopers (PwC) which provided independent reference of survey data analysis validity (Makower J., Meer A., Denend L., 2010). Another one performed by PwC itself together with life science association BIOCOM surveyed 50 companies within the life science sector, 19 of them producing medical devices (the rest of respondents represented manufacturers of pharmaceutical, biologics, providers of clinical research services and cell-based therapy) (PwC & BIOCOM, 2010).

The authors of the first report, referring to Ernst&Young’s recently acquired data, suggest that there are about 1000 active medical device manufacturers in the US, which indicates that the survey is based on a representative sample of companies, at least with regards of their number (Makower J., Meer A., Denend L., 2010). The survey included such parameters as: time and cost required to get through approval on both markets, as well as competence of regulatory authorities, predictability of their requests, their reasonableness and transparency, and overall experience of the companies with US and EU authorities.
The study results suggest that the same devices get approved on average two years later in the US than in the EU, in some cases this so-called “device lag” is as much as six years (Ibid). The results for other parameters are shown in the table 1 below.

Table 1. Results of the survey conducted by Makower et. al. (Makower J., Meer A., Denend L., 2010, p. 24): the percentage of respondents which assess the performance of each of authorities as “highly or mostly” competent, transparent, predictable or reasonable, as well as answer “excellent or very good” referring to their “overall regulatory experience”.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>US</th>
<th>EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical competence</td>
<td>47%</td>
<td>88%</td>
</tr>
<tr>
<td>Engineering competence</td>
<td>52%</td>
<td>91%</td>
</tr>
<tr>
<td>Statistical competence</td>
<td>60%</td>
<td>79%</td>
</tr>
<tr>
<td>Predictability</td>
<td>22%</td>
<td>85%</td>
</tr>
<tr>
<td>Reasonableness</td>
<td>25%</td>
<td>91%</td>
</tr>
<tr>
<td>Transparency</td>
<td>27%</td>
<td>85%</td>
</tr>
<tr>
<td>Overall experience</td>
<td>16%</td>
<td>75%</td>
</tr>
</tbody>
</table>

The trend of decreasing performance of FDA has been observed during past several years. As for the costs that manufacturers bear in form of regulatory fees and money required simply for keeping the company afloat while the pre-market review is carried out, the overall sums are reaching alarming limits in the US, which negatively influences the investment climate in the industry. Entry to European market is available at a lower cost (Ibid).

The other study respondents are pointing at somewhat improved relationship between the industry and FDA, although this improvement is also less apparent than four years earlier. However, they also mention inconsistency of FDA position in reviewing applications (60% of respondents) and denials in approval caused by lack of resource possessed by the Agency (40% of respondents) (PwC & BIOCOM, 2010). The findings of this report are further discussed with more close relation to namely medtech industry in PwC report: Medical Technology Innovation Scorecard (PwC 2011) and, in consistence with Makower’s study, indicate that the same technologies get approvals on both markets, though US approval takes about two times longer. According to PwC survey the US process is also deemed less certain and predictable than the European one.

6.3.2 Output ability of the US and EU regulatory systems to ensure public safety

Reasonable question arises accordingly: whether the relative efficiency of the EU approval process compromises its effectiveness, i.e. the devices’ safety and influences the public health protection negatively. In this connection the recent debate between American and European officials worth mentioning, in which Jeffrey Shuren, the head of CDRH department at FDA declared that the European system treats the public as “guinea pigs”, accusing it in insufficient measures to protect the population. This statement provoked a quite strong reaction of European officials, asking FDA to share the evidence supporting such allegations with the European side (Blair T., 2011).

Indeed, the existence of such proof seems to be doubtful. Recent study conducted by Boston Consulting Group (BCG) implies that the overall recall rates in the US and EU are generally the same (Davis S., Gilbertson E., Goodall S., 2011). Referring to this report in his Statement before the Subcommittee on Health Committee on Energy and Commerce,
US House of Representatives Shuren argues that the report conclusions may be untrustworthy (Shuren J., 2011), keeping in mind that the data on recalls are not equally collected throughout Europe and the majority of these data come from five member states out of twenty-seven. However, the study methodology included the data standardization and defining the number of unique recalls by company name and therapeutic group (Davis S., Gilbertson E., Goodall S., 2011).

Furthermore, as mentioned before, generally the same technologies get approved in the US and EU, although with a time lag (Makower J., Meer A., Denend L., 2010, PwC 2011). No safety issues have been a subject of groundbreaking discussions in media (Blair T., 2011) and Shuren himself does not provide any figures of just how many devices approved in Europe are rejected in the US and how many of them have caused serious problems, mentioning just one such a case (Shuren J., 2011).

So, although further research is required on this matter, it can be concluded so far that European procedure ensures reasonable safety level, which has not been shown to be lower than the American counterpart provides.

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although in general the involvement of stakeholders into enforcement of desired path of institutional development should benefit the institution’s efficiency, in the case of FDA it contributed to the opposite, forcing the Agency taking up the defensive position. The reason of such an effect is likely to be the stakeholders’ low ability to measure, i.e. understand the environment.

The data further suggest that due to increasing shortage of resources and technological complexity of device submissions, FDA has recently reached its performance capacity limits, which is illustrated by rising dissatisfaction of the stakeholders. Furthermore, as both complexity and resource constraints are likely to continue increasing, performance will continue falling, which calls for reconsidering the current regulatory approach applied at FDA, very possibly including some trade-offs with the industry.

European system is more agile and shown to handle changes more effectively, being built on the base of standardized requirements to the industry. It makes the European approach more predictable and transparent, as well as the approval process less costly, which is a strong point in attracting venture capital to Europe.
7 Impact of medical device regulations on current and future industry landscape

7.1 Factors determining competitiveness of regulatory approaches

Innovation in medical technology is often looked upon as the most promising source of tools which would be able to cut the Gordian knot of quickly rising health care expenditures reaching now critical level in majority of national economies (PwC 2011). Consequently, the country or region which can create the most supportive environment for innovations in this field and attract manufacturers to launch their products for the first time there will get direct benefits in form of better and cheaper patient care and more advanced health care system. Further selective advantages such as rising experience of health care system with innovative technologies and competence leak to these markets are fueling next generation of innovations (Makower J., 2010).

Medical device regulations, in their turn, are an important part of innovative ecosystem of the medtech industry (Gollaher D., Goodall S. 2011, Makower J., 2010) and one of its bottlenecks (PwC 2011). Lacking the developed and supportive regulations within national borders is the key factor of structural tension within medical technology development block and those countries that develop policies to overcome these difficulties will be leading the sector in the future.

The majority of the companies populating the medical technology industry are small manufacturers strongly dependent on venture capital to get their technologies on the market (Gollaher D., Goodall S. 2011). From the point of view of VC, not the level of regulatory scrutiny, but rather time the approval is taking, transparency and predictability of pre-market review are the main factors of to regulatory regime which determine the success of investment. Predictability is more important than review times, as even longer time can be planned, but if the approval process is not predictable and consistent the risks get unmanageable. However, timing is also an important factor, keeping in mind that for revenues to start coming in the device needs to not only be approved but also built into reimbursement system, furthermore the technology needs some time to diffuse (Feigal D., 2010). Especially critical these variables get in the situation of financial recession (Makower J., Meer A., Denend L., 2010).

Also, medical technology is much more complex as a product group than pharmaceuticals in terms of sizes, technologies applied and diversity of their intended use. New device is different from a new drug. Innovation of medical devices is going on incrementally, accelerating, not impeding with time, and one device can undergo several cycles of modular innovation, producing next generations of technology and occasionally technological transformations (Hiderfjäll P., 1997). Completely new, high-risky products are of the greatest potential for the future ratio of healthcare costs and availability. Therefore, another important factor is that regulatory approach should be robust in order to address equally well the whole range of medical technology products, and specifically taking into account incremental character of medical technology innovation.

Basing on the results of analysis performed in the present study it is possible to:

a) Highlight the particular features of US and EU approaches that are key to support the innovative ecosystem, i.e. those which determine efficiency (the level of transparency, predictability, timeliness and robustness) of corresponding regulatory approval process.
b) Make assumptions regarding the future paths of US and EU regulatory systems development, basing on previous history and current environmental influences and try to predict if these regulations will be more or less supportive in the future.

7.2 Traits of US and EU regulatory approaches determining their efficiency

The analysis suggests that the European system is on a par with American one when it comes to ensuring public safety. Even keeping in mind remaining issues of standardization of the work of Notified Bodies and creation of all-European market surveillance and vigilance register, initial level of safety requirements on the European market is advanced.

As for the indicators of efficiency of the regulatory approach, i.e. the level of its transparency, predictability, timeliness and robustness, European system outperforms American one. Moreover, the future trend is towards further increase of the gap between the two systems' performance. Therefore, it should be appropriate to look into European approach and point out which of its traits provide its better efficiency.

The main source of predictability, transparency and robustness of European approach is the use of standards, which proved to be an elegant tool to scale the diversity of the industry. Pure risk-based classification of devices serves the same purpose. Using both classification and abundance of standards available for a wide range of different purposes applicable standards can be chosen for each case of device. The trick is that standards pre-exist the approval submission and their requirements do not depend on the particular device features and complexity, only the number and the choice of applicable standards do. Therefore, it makes all the devices to be regulated according to the same generic rules, which removes the human factor from assessing submissions and is a pre-requisite of predictability, transparency and robustness of the approach.

Timeliness is not an exception: if generic rules are applicable to the whole process the review will take less time. However, with regards of timeliness the resource issue should be mentioned. Even such a huge and powerful organization as FDA cannot afford the amount of resources and competence the professional community can offer, especially keeping in mind the amount of responsibilities FDA is granted with. Under pressure of rising environmental complexity borrowing competence from outside the state and diversification of responsibility among several different actors in general seems the most apparent solution to the problem of constrained resources and, subsequently, ensuring timeliness of approvals.

7.3 Future paths of US and EU regulatory systems development and further implications

Although US continues to be the leader in medical technology, EU has improved its positions during last several years due to its robust and contemporary regulatory system which is an important instrument of learning on this market and, therefore, a link in a set of institutions fueling the innovation ecosystem of the medical technology industry.

Returning to the theoretical discussion, effective institutions should develop together with industries, however they are subject to positive feedback rules and tend to lock in a certain path, not necessarily optimal. And in case if inefficiency of supporting institutions is observed the reform may be required.
American system seems to be a product of its evolution from 1976 and even earlier years, keeping in mind that FDA had performed the regulation of pharmaceuticals long before MDA assigned it to regulate the medical technology as well. In the current situation of decreasing performance of the Agency and increasing dissatisfaction of various stakeholders the change in its approach is required.

It would not be wise, however, to call for deregulation, which can be harmful for one of the most profitable industries. As we could see, the regulation design is a different thing with its implementation. The first thing that could be done to improve the performance of American system is to place more emphasis to use of harmonized standards applied to regulatory approval. Second, the information deficiency should be addressed, i.e. research legitimating the current path of development should be systematically arranged and its results actively broadcasted. As discussed above, FDA bureaucracy is highly inert and reluctant to change if it is proposed from outside the Agency, however, if all its actions are properly legitimated it could ease the pressure on FDA, letting it work more consistently. Such projects as Mutual Recognition Act: the document signed in 1998 between US and EU for delegation of authority to several selected bodies to perform approvals in Europe on FDA's behalf and in US on European authorities' behalf (Dickinson J., 1997) should be continued and implemented.

European Union has built the regulatory system on the base of American philosophy. However, European regulators managed to leave behind the inefficiencies embodied in American approach. The current EU approach has its shortcomings, e.g. instruments accreditation of Notified Bodies and keeping recall records should be improved, but those issues are lying on the periphery of the approach, rather in its core, i.e. can be fairly easily improved.
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