

**EU Regulation of Medical Devices and Pharmaceuticals  
in Comparative Perspective**

by

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## Introduction

In their article referring to the ‘constitutional asymmetry’ in European Union (EU) policy-making<sup>1</sup>, Permanand and Mossialos (2005) seek to explain why, despite the existence of a Community regulatory regime for pharmaceuticals for some thirty years<sup>2</sup>, there is still no single European market in prescription drugs. At the core of their explanation is an alleged ‘clash’ between the supranational free movement rules (the driving force of industrial policy, which is preferred by the relevant stakeholders) and national health policy competencies (which, under the principle of subsidiarity, sees certain policy competencies undertaken at the lowest level at which they can best be pursued). An additional complication is that this clash takes place against the backdrop of limited public health advocacy at EU level. Though launched some thirty years later as an integral part of the Single European Market (SEM) project during the late-1980s, medical device regulation faces similar conditions. Market-biased EU rules for industrial and trade policy, which are reinforced by Treaty-based provisions and free movement-oriented rulings of the European Court of Justice (ECJ), exist in tandem with weak EU public health competencies. For both sectors, therefore, despite distinct and more or less legally and procedurally unified EU regulatory frameworks, there is still no EU-wide market in the manner of other more traditional industrial products. The purpose of this paper is to compare EU medical device and pharmaceutical regulation and policy, and to ask why and how the two regulatory regimes differ.

Our comparison proceeds in several steps. We first outline the issues that we aim to clarify in analyzing the similarities and differences between the regulatory regimes for medical devices and pharmaceuticals. Next, in addition to the ‘clash’ between economic and social imperatives, we address another paradox in the regulation of the two sectors; namely, that despite the proliferation of EU competencies, national level regulation has in

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<sup>1</sup> This refers to the EU’s comparatively well-developed economic policy competencies versus its less-developed social policy mandate.

fact increased. We then seek to ground the comparison in pertinent scholarship on EU integration and policy-making, before then highlighting regulatory differences in reference to the ‘regulatory life cycle’ concept<sup>3</sup>. This helps set the backdrop to exploring in detail the reasons for the differences between the two regimes. By way of conclusion, we will draw out the empirical lessons learned. Ideally, they will form the basis for theorizing about this topic at a later stage.

## **1. A common constitutional-institutional framework – yet different regulatory regimes**

The pharmaceutical and medical device industries are both indispensable to the delivery of health care and clinical innovation, and not just in Europe. Both manufacture products that are highly sensitive, and which represent vital public goods that play an essential role in the provision of health care, the restoration of health and well-being, and the avoidance of premature death. Drugs and medical devices are crucial for clinical research and innovation, yet both can pose severe risks to human health if they are poorly regulated or inappropriately used. Thus, the object of regulating drugs and medical devices is not only to promote their international and regional trade – and to enhance the competitiveness of the European industry – but, above all, to serve public health needs. More specifically, they must meet the objectives of safety, quality and efficacy – the three regulatory approval ‘hurdles’ – upon which national health protection schemes and healthcare systems have come to rely (this also raises the issue of the so-called ‘fourth’ and ‘fifth’ hurdles in the interest of regulating for public health and patient safety<sup>4</sup>). To meet these and other expectations the EU has set an extraordinarily ambitious policy objective for public health and consumer safety generally. Not only does the EU aim to “promote the interests of consumers and to ensure a high level of consumer protection”,

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<sup>2</sup> According to Hollingsworth et al (1994: 4) “a regulatory regime covers the totality of institutional arrangements—including rules and rule-making agents—that regulate transaction inside and across the boundaries of an economic system.”

<sup>3</sup> This follows the OECD’s broader understanding of regulation, or *regulatory management* (1997), that covers all phases in the ‘regulatory life cycle’.

<sup>4</sup> The fourth and fifth hurdles are that of clinical effectiveness and cost-effectiveness/affordability i.e. whether the proposed drug is, in clinical terms, better than existing products, and whether it is affordable and good value for money.

the Community shall [also] “contribute to protecting the health, safety and economic interests of consumers.” Moreover, “a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities”. Policy rhetoric aside, realizing these goals is an on-going process of learning by doing and seeking consensus through compromise and conflict resolution, and the medical device and pharmaceutical sectors represent cases-in-point.

In terms of the EU policy environment, both sectors are exposed to similar EU interventions according to Treaty-based competences and ECJ court rulings. Moreover, they are subject to similar European level conditions – constitutional, political, institutional and economic, as well as judicial (independent variable) – regarding market access, international trade relations and regulatory convergence, and the competitiveness of industry. Nevertheless, important differences remain. Are these similarities and differences the result of the differences in timing at the start of EU regulation in each sector? Or is the divergence related to the power of the stakeholders which control the respective EU and national ‘regulatory space’? Do political and institutional traditions unique to each regulatory regime explain the differences? Should variations in stringency be anticipated as a result of some fundamental differences in the nature of drugs and medical devices? Finally, do these differences stem from the respective interface with national health protection schemes and the way they are treated as covered and reimbursable items? Through process-tracing each phase in the regulatory life cycle, this paper aims to address such questions, and will do so by connecting insights from three distinct academic traditions: political science, EU studies, and health policy research. Our comparison necessitates a multi-disciplinary approach that combines conceptual and more applied social science.

In attempting to understand this situation, therefore, rather than engaging in a theoretical discussion, this paper aims to explain what these differences are, to identify their root causes, and to consider the implications for knowledge about European public policy (which is inherently comparative). Our comparison is theoretically modest, and we instead look to address an empirical gap as a first step. Beyond the issues raised

above, we are primarily interested in the answers to two crucial questions. First, why, despite more or less uniform market-access conditions on the one hand, and an equally central role in the member states' respective national health protection schemes on the other, does empirical research on pharmaceuticals and medical devices point to a number of unexpected differences between the two sectors while at the same time revealing few expected similarities? Second, what is there to be learned from a comparison of EU regulation of medical devices versus that of pharmaceuticals? To the extent that problem-driven empirical research produces descriptive material, and enables us to identify patterns of behavior, action, and procedures, this paper should be considered as a first contribution to theory development about EU regulatory policy at a later stage.

There are many ways of engaging in a comparison. In contrasting and comparing similarities and differences in stringency of regulation we will also explore the balance struck between trade and international competitiveness and public health and health care policy objectives in the European Union. Permanand (2006) has adopted this three-part policy-balancing approach to examine EU pharmaceutical policy, and we find this framework as a useful backdrop to be borne in mind through out the discussion. We thus incorporate the key characteristics that best describe the core activities in each policy sector. Table 1 captures a first set of commonalities, to which we will return at a later stage.

**[INSERT TABLE 1: Interface of Industrial Policy with Healthcare and Public Health]**

## **2. The 'paradox' of regulation and the CE marking system**

This 'clash' or asymmetry between coherent EU rules in favor of trade and competition and the heterogeneous objectives and rationale of national health protection schemes, is compounded by another paradox reported for EU product regulation in general<sup>5</sup>. Namely, that despite much regulatory reform – through mutual recognition of

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<sup>5</sup> According to Laid and Yeats (cited in Hanson 2005) "Between 1981-1986, the number of non-tariff trade barriers increased in Germany by 36 per cent, in France by 30 per cent and by 24 per cent in the EU as a

the equivalence of technical standards and testing and certification procedures, including confidence-building measures, approximation, and other means – and the liberalization of the European market over the last 25 years or so, the trend in national product regulation of foodstuffs, pharmaceuticals and medical devices has actually increased since the mid-1980s in the push towards the single market (Pelkmans et al 2000, Joerges 1999). For prescription drugs this is evidenced in the increasing number of notifications to the Commission per year, and the fact that national regulatory activities have not ceased (Pelkmans et al 2000). For medical devices, the regulatory situation and the evidence are similar. A member state which plans to require higher public health standards in any new legislation has to notify the Commission about such intentions, notably when such a new provision may run counter to EU stipulations. In the case of medical devices notification can concern, first, conformity assessment with ‘Essential Requirements’ (ERs)<sup>6</sup> and, second, standards – medical, diagnostic, therapeutic – as stipulated in the ERs (Cutler 1998). ERs play a more important role in regulating medical devices than medicines; this because of the considerable diversity in type, application and make-up of medical devices. For medicines, whether approved centrally via the European Medicines Agency (EMA) or nationally via the member states’ own regulatory agencies, manufacturers have to submit a Summary of Product Characteristics document outlining in detail the product’s properties and conditions attached to its use. It is on the basis of this report that regulatory authorities make their assessments. In the case of products approved via the EMA, a member state can only object to an authorization being granted for its market on demonstrable public health grounds. More common, as reported by Abraham & Lewis (2000), is that some national authorities have accepted EMA-approved drugs that their own national authorities might otherwise have rejected.

Individual national requirements were to have been phased out by 1992 with the launching of the single market project in 1986 via the Single European Act (SEA).

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whole.” Hanson (2005) puts the creation of most of these barriers down to inconsistent national product requirements.

<sup>6</sup> ERs, which are stipulated in great detail in annexes and non-binding guiding documents concerning the Medical Device Vigilance System in the European Union (MEDDEV documents).

According to Pelkmans et al (2000), and other analysts (Hanson 2005; Armstrong 2002; Cutler 1999; Higson 2002) neither ‘approximation’ nor ‘mutual recognition’ work satisfactorily. Yet they are crucial enforcement tools and are at the heart of the *new approach* initiated in 1986 with the SEA. The essence of the *new approach* to product safety regulation through harmonization and technical standardization is two-fold: first, the development of modules specifying regulatory requirements, ranging from design and quality to the manufacturing process, and based on international standards (ISO series); and second, private commercial certification authorities (so-called ‘notified bodies’) which certify the conformity of the products in line with EU regulatory requirements based on the self-declaration and the documentation submitted by a manufacturer. That mutual recognition does not work for drugs and medical devices in the way it does for more traditional industrial products is not difficult to understand.

In drug and device regulation, mutual recognition addresses extremely sensitive issues such as the exchange across borders of clinical data, patient information, and confidential data about innovative and research and development (R&D) processes at the interface of clinical researchers and manufacturers (protection of intellectual property). Mutual recognition also concerns industrial data on manufacturing processes (trade secrets and protecting commercial secrecy) along with clinical trials for market approval. When regulators want documentation in support of submissions for market approval, and they require evidence that products are safe and efficacious based on clinical evaluation data, they touch on confidential issues and provoke strong resistance by the industry, trade associations and professionals alike. The issues become exponentially more complex when efficacy is defined in terms of improved clinical outcomes for a new device or drug over an existing product already on the market; this is often based on the manufacturer’s claims, though not necessarily evidence. The term ‘technical standard’ also hides complex scientific issues which vary greatly for equipment, for drugs and for medical devices in terms of complexity, sensitivity, expertise and final outcomes on patients’ health. For medical devices we thus speak of medical, diagnostic and therapeutic standards.

As to conformity assessment, Hanson (2005) finds no single pattern: “conformity assessment requirements may range from nothing, to self-declaration by a manufacturer, to a requirement that a third party must review the design, certify the manufacturing processes or test the finished products” (6). If a product conforms to EU requirements, it will be CE-marked. Yet ‘uniformity’ is not the same as liberalization and, according to one European CE expert, “the implementation of the CE marking system has too often been based on the more restrictive national regulatory systems rather than the less restrictive systems.” (Messelin cited in Hanson 2005: 39)

Along similar lines, Egan (2002) explains that the EU was faced with a classic problem of a regulatory mismatch: the tools available to limit the impact of national product standards and conformity assessment requirements on the internal market were not appropriate for achieving the desired goals. According to Hanson (2005), the ‘old approach’ to product regulation has been widely regarded as a failure. The pertinent literature speaks of a lack of expertise and considerable delays, but also of disagreement among the standard-setters which hampered progress. Hanson thus contends that the more ‘protectionist interests’ at national level were able to undermine the more liberal EU level policies. And, as a result, the CE marking system was watered down such that the Commission’s ‘new approach’ directives were less contentious, with implementation decentralized, and industry and national governments having been accorded a major say.

Product safety policies are made at EU level but their implementation is subject to home country control (because of the subsidiarity principle). Given the extent of decentralized regulatory implementation, EU unified product markets for medical devices and pharmaceuticals would never translate into uniform implementation conditions in the member states. Subsidiarity entails two structural conditions. First, EU policy-making relies for implementation capacities almost entirely on public and private implementation structures in the member states. That is, national governmental agencies, standards developing organizations, commercial auditing and certification companies, and European industry. Second, that the burden of regulation is placed on manufacturers and health facilities to adapt to new legal principles. European Union law, like national law,

does not secure automatic enforcement and implementation in the member states. Regulatory implementation is mediated by institutional arrangements and the politics of stakeholders which influence, though they do not determine, the final outcomes. In view of highly variable institutional conditions in the member states, it should not come as a surprise that much empirical analysis of the implementation process shows significant variations in response to one and the same set of EU provisions across the member states. This is true not only for amply researched policy sectors such as pharmaceuticals, telecommunications, transport and the environment (Héritier et al 2001) but also, and possibly more so, in less researched policy domains such as the medical device sector.

### **3. A common theoretical framework**

In continuing our look at medical device and pharmaceutical regulation, we turn now to contextual factors which might contribute to the differences between the two sectors. Here we find the broader-ranging EU policy environment work of Andersen and Eliassen (1995) and Scharpf (1999) useful in helping us to identify key issues relevant to understanding the different regulatory trajectories of the two sectors – the former is grounded in sector specific analysis and the latter in a wider public policy approach. Recognizing the importance of sectoral variations within the European Community, Andersen and Eliassen asked which institutionalization forces were strongest in explaining this: ‘EU institutions, national traditions, policy sector traditions, or issue characteristics.’ Scharpf meanwhile raised the broader question as to whether generalizing about European public policy across policy sectors is feasible and meaningful. His observation is unusual but significant. Speaking to ‘theory-oriented students of public policy in Europe’, he writes:

There is no reason to expect that *general* propositions will explain and predict either the impact of economic integration on the national governance capacities, or the capacity of European or international institutions to deal effectively with problems in those areas where national solutions are in fact undermined. Thus, the fact that existing empirical studies come to widely differing conclusions, some highly optimistic, others deeply pessimistic, need not imply that at least some of

these authors must be wrong. Instead it is quite likely that the cases studied are dealing with different constellations in which different outcomes should be expected. Thus, if research should not merely provide descriptions of the empirical variance, but aim at theory-based explanations and predictions, it will be necessary to identify those differentiating factors and causal mechanisms that affect the outcome one way or another. (116)

To gain a realistic appreciation of what Scharpf calls the differentiating factors and causal mechanisms of regulation of products across the two sectors, the ‘regulatory life cycle’ concept is also useful in helps us to understand broader elements which impact on the orientation of regulatory policy.

Our question, therefore, is what are the significant phases in the regulatory life cycle of drugs and medical devices? In general, these include the regulation of design and manufacture, quality controls, other pre-market controls, sales, advertising, as well as post market controls. Post-market controls are composed of two distinct sets of controls which concern two different audiences. Surveillance and post-sales responsibilities target manufacturers, while pharmacological and medical device vigilance and adverse incident reporting target both manufacturers and an array of medical professionals (and of course based on public health needs and patient experience specifically). Admittedly, this is a simplification and does not cover all phases in the cycle. But it is useful for our purposes in providing grounds for a comparative indication.

Presumably, some ‘causal factors’ may lie in the respective EU regulatory frameworks, some in their interface with the national health protection schemes, and yet others in their being an integral part of national healthcare systems. We need to look at each phase of the regulatory life cycle in order to identify the empirical factors that allow us to differentiate between pharmaceutical regulation and medical device regulation. This approach forces us to acknowledge that not only are there major differences between the two sectors, but that regulation itself is not a unitary process. Rather, the multitude of political forces at work involved during one phase may not be reproduced in another phase. Distinct dynamics and vested interests may come into play in each phase – R&D

for drugs and medical devices, their manufacture, the drafting of EU rules on packaging, labeling, advertising, sale, and, above all, their use, and disposal all involve different processes (Cheng 2003) – and so too different political, economic and professional pressures. In considering the life-cycle phases mentioned above, therefore, three distinct phases emerge: (i) *pre-market controls* (the regulatory requirements for getting products approved and licensed for sale on the market (ii) *post-market controls* (understood as manufacturers’ obligation to operate a system for obtaining feedback from the marketplace) and (iii) *medical vigilance* (understood as the obligation to report serious adverse health incidents to the competent authority; that is, quasi autonomous regulatory agencies in the EU member states).

The rationale for engaging in what George & Bennett (2004) term a ‘structured, focused’ cross-functional comparison, is to go beyond the conventional wisdom that treats regulation as a unitary process and considers regulatory details as highly technical and of no interest to political science. But how can we say anything empirically meaningful about the quality and efficiency of regulation, as well as the similarities and dissimilarities of regulatory policy concerning two product sectors, unless we specify sector-specific items and variations across the two. Aggregate data (document, statistical and other) tend to mask substantive differences in the nature of drugs and devices. Often the assumption is made that a similar dynamic drives the politics of the respective stakeholders and regulatory agencies and their interactions. Yet there are studies that point to important differences in the approaches chosen for regulating drugs and devices on the one hand, and on the other distinct national approaches to regulating coverage and payment mechanisms by the payers in the member states on the other. Finally, there are crucial differences in the professional dynamics between providers (clinicians) and vendors that come into play.

#### **4 Commonalities and differences**

As already noted, drugs and medical devices are indispensable for the delivery of health services, and while patients/consumers can therefore be seen as the main

stakeholders – at least in theory – there are a host of other actors and interests involved in the respective sectors and are affected by their regulation. In this vein, Table 2 provides a sketch of the main interested or affected parties and entities for medicines in any given national environment, but they are relevant to medical devices as well.

**[INSERT TABLE 2: National Actors and Policy Objectives in the Pharmaceutical Sector]**

The table is an admittedly simple one. However, it is useful to our discussion for three reasons. First, it makes the connection between EU regulatory policy-making and health services, along with its wider environment. Second, we are reminded that regulatory policy-making is executive and top-down, relying for its enforcement primarily on organizational actors. In this way regulatory policy also reveals a high degree of functional diversification of tasks and targets. Finally, the table helps to disentangle the panoply of key actors involved in pharmaceutical politics – or are the targets of pharmaceutical regulation – and by extension for medical devices as well. For it highlights that there are key actor groups at the macro and micro-levels, both of which need appeasing through regulatory outcomes. The analysis by organizational entities also helps to identify a more diverse set of organized actors than is usually anticipated in theoretical research. If we were to add the supranational dimension to the table, we would find that several EU bodies are involved, including individual elements within them (e.g. different Directorates-General in the Commission, the European Parliament and its various committees, etc), along with EU level trade associations and representation groups for industry, doctors, patients, and consumers. We here wish simply to highlight that there is a considerable number of vested interests involved in both sectors, with sometimes opposing policy interests, all of which need to be met in the regulatory outcomes agreed at national and supranational levels. There is clearly a higher degree of sensitivity involved in medicines and devices than in other, ‘simpler’ industrial sectors, and this is to be borne in mind whenever undertaking a discussion about either sector.

#### ***4.1 Historical trajectory***

The two sectors have been evolving under the broader EU umbrella of the ‘constitutional asymmetry’ in policy-making. They benefit from the similar driving forces (economic, political and legal), yet also suffer from similar constraints: trade-biased EU rules, the absence of EU public health competence, and the existence of national health protection schemes, as well as highly competitive and irreconcilable diverse policy objectives. There is one significant difference, however, and it is the timing of institutionalizing a regulatory regime. The historical trajectory of pharmaceutical regulation precedes that of the medical device regime by some 30 years when it was embedded in ‘old approach’ legislation. Although the old approach was insufficient to push the emergent single market agenda forwards – indeed, the bulk of pharmaceutical legislation was prompted by the need to be ready for the single market deadline of 1992 – it did set important regulatory requirements for pharmaceuticals which are still in force, even if their scope is otherwise limited (Hanson 2005). This includes both the approval criteria for new medicines – the very first piece of EU pharmaceutical legislation laid down safety, quality and efficacy as the sole approval criteria – and the origins of a single authorization for multiple markets within the EU. The *Thalidomide* tragedy prompted the Commission’s initial move into medicines policy under the old approach, and it is this public health basis which remains at the heart of EU competencies, even under the new approach.

In contrast to the public health protection origins of EU pharmaceutical policy, the historical trajectory of medical device regulation is deeply embedded in the market-building project in the mid-1980s, continuously evolving and characterized by surprises and unexpected developments which erupted in occasional political storms and conflicts over unresolved regulatory issues. The thorniest of all has been the French opposition to the application of the EU approach on CE-marking from 1990 to 1998, and the political debates over setting up a European agency on medical devices separate from the EMEA. The relevant stakeholders pursued a political and legal strategy for establishing an EU-wide legislative regulatory framework for medical devices that was to be separate from the older pharmaceutical regime. All so-called ‘borderline’ products – such as drug-

device combinations – came under the medical device framework. To the extent that some member states regulated medical devices prior to EU legislation or competencies, these remained under the national pharmaceutical regimes or, alternatively, came under the Europeanized medical device regime for the first time in many other member states. EU regulation of medical devices proceeded on the basis of classifying medical devices by risk categories.

**[INSERT TABLE: 3 Synoptic Timeline of EU Pharmaceutical and Medical Device Regulation]**

**4. 2 *The industry***

According to Greenwood (1995: 286-287), the pharmaceutical and the medical device industries control ‘key resources’ in the EU: (i) effective organizations for representational purposes; (ii) resources that are of a strategic nature to the people of the European Union; (iii) EU competencies in the policy domain; and (iv) politicized issues. Control over these resources offers dual payoffs: at the EU level insider status for drafting new rules and setting new standards (not only engineering but also diagnostic, therapeutic and medical) through advisory committees convened by the Commission; at the national level, governments and payers are attempting to stem the rising tide in health care costs. For details of the profile of each industry, in other words, of their power and influence, see first entry in Table 4 below.

It is the case that the European medical technology and medical devices industry is not as powerful and significant as the European pharmaceutical industry in terms of production, resources, sales turnover, profits, or employment and knowledge. Pharmaceutical firms had the status of national champions two decades ago, receiving special protection from national governments. In contrast, there were never were any national champions in medical devices, except perhaps for Siemens and Philips. After going it alone since the late 1990s, EUCOMED now is closely cooperating with the US-based AdvaMed (previously HIMA). In part they are pursuing similar interests in promoting the adoption and diffusion of new technologies, and EUCOMED needed the

lobbying skills and experience of AdvaMed in order to impress their preferences on the Commission.

Prior to the mid-1980s, most medical device manufacturers operated in national non-integrated markets where manufacturers, suppliers and distributors ‘learned the ropes’ of operating within NHI or NHS healthcare systems and how to adapt sales and marketing strategies to the regulatory regime extant in each country. Friendly relations with health administrations and public insurers and payers provided significant advantages, and could create monopolies over supply and distribution (such when a manufacturer insists that distributors only carry their products under their conditions they stipulate). The post-war expansion period from the mid-1960s onward ended with the creation of a single European market.

#### ***4.3 ‘Differentiating factors’ and ‘causal mechanisms’***

The major properties and differences in the nature of drugs and medical devices are summarized in Table 4 below. In the following section, we examine in more detail the reasons for the different regulatory trajectories followed by the two sectors.

**[INSERT TABLE 4: Differences in the Nature of Drugs and Medical Devices]**

##### **4.3.1 The pharmaceutical sector**

The first European (Economic) Community legislation specific to medicines came in 1965. In view of the then recent *Thalidomide* tragedy, policy-makers sought to agree common regulatory controls and standards on new medicines in order to protect public health. Directive 65/65/EEC thus defined a medical product as:

...any substance or combinations of substances presented for treating or preventing disease in human beings or animals or any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or animals.

And classified a proprietary medicine as “...any ready prepared medicinal product placed on the market under a special name and in a special pack”. The Directive further established guidelines on the development and manufacture of medicines and set out safety, quality and efficacy as the criteria for market approval. Any industrial or economic interests were thus to be second behind the public health concerns. By the mid-1970s, however, with closer economic ties developing between member states, industrial and cross-border trade issues began to creep into policy-makers’ concerns.

In 1975 came Directive 75/318/EEC. This created the ‘mutual recognition’ procedure for approving new medicines: a product granted marketing authorization in one member state could now be granted automatic multiple authorizations without the company having to file a separate application in each state. The Committee for Proprietary Medicinal Products was also established as the central authorization body for the Community market. The idea was to promote cross-border movement of medicines in keeping with an established free trade area. However, Article 36 of the Treaty, which allowed member states to raise objections to products being released onto their national markets on the basis that the products could have a negative health effect, meant that the mutual recognition procedure did not speed or foster authorization as hoped. The member states constantly raised objections to those medicines approved in other member states and which the Committee had approved for extension to their market. Moreover, the manufacturers, unhappy with the resultant delays, generally chose not to use the procedure, preferring to apply to each country separately despite the extra bureaucratic requirements. Revised legislation was therefore not long in coming. In 1983 Directive 83/570/EEC introduced the ‘multi-state’ procedure, under which the minimum number of countries to which authorization would be automatically extended was dropped from five to two. Although more successful than mutual recognition in terms of the number of applications submitted by the industry (companies often had reasons for wanting to launch in only some member states, and only at specific times), the member states continued to remain skeptical of each other’s assessments, and again raised objections to medicines approved via the new procedure. The multi-state procedure too failed to

deliver on the European Commission's aims at improving and streamlining the regulatory approval process for medicines in the EC.

The wider backdrop to this increasing interest in pharmaceutical regulation were discussions towards the 1986 Single European Act (SEA). The SEA formalized the aim of establishing a Single European Market for the free movement of all goods, services and capital by 1992. Towards this end, the SEA was soon followed in 1988 by the Cecchini Report, which looked at the current state of affairs in terms of the readiness of individual sectors, and sought to highlight the benefits of a single market (Cecchini et al 1988). The report picked out pharmaceuticals as a problem area because of their being "irretrievably linked to public health" and thus an issue of national sensitivity. At the same time, again with a view to streamlining the approval process for medicines, however, Directive 87/22/EEC was agreed in 1987. The legislation set out a new 'concertation' procedure, which was relevant only to biotechnologically-developed and other high technology products: manufacturers were required to simultaneously submit their applications to the committee and a single member state, and once each had completed their evaluations, together they facilitated discussions between the applicant and the other national authorities.

In addition to improving the efficiency of Community medicine approvals, another Commission priority was to address the issue of price differentials on medicines between the member states. According to Chambers and Belcher (1994), this was up to five times on a single product during the mid-1980s, and other sources put it even higher. Setting medicine prices remains a member state competence as an integral part of national healthcare policy, and the Commission has no influence here. In hoping to instigate some impetus towards a gradual diminishment of the price differentials, the Commission was able to secure agreement on the so-called 'Transparency Directive' in 1989 (Directive 89/105/EEC). The Directive obliged member states to adopt 'verifiable' and 'transparent' criteria in setting prices and their reimbursement under national health insurance systems. Although not affecting prices per se, this was to ensure that no collusion between industry and government over prices was taking place, and to make

sure that no discrimination against medicines imported from elsewhere in the EC was taking place. This was an attempt by the Commission to address the pricing issue in reference to the 'free movement' provisions.

Further legislation pertaining to labeling and packaging, patent protection, advertising and sales promotion, and wholesale distribution followed (Directive 92/27/EEC, Regulation 1786/92, Directive 92/26/EEC, and Directive 92/25/EEC), and was aimed at serving the free movement requirements of the single European market. With price differentials continuing, the Commission sought to achieve consensus with the member states over the need to promote the European pharmaceutical industry more generally – it was hoped that this would, indirectly, lead to some form of price harmonization at a later stage. Thus, in 1996 came a document outlining the development of an EU industrial policy for pharmaceuticals (Resolution 96/C136/04). The document was agreed as a Resolution rather than a Directive or Regulation – with no legislative authority – and has not been pursued. Without going into the details, the point to be made is that, as of now, it was clear that single market priorities had come to dominate the Commission's thinking in all policy areas, including medicines. Industrial and single market policy concerns, rather than public health protection interests, had thus come to be the main influence on the Commission's pursuit of further regulatory policy competencies in the pharmaceutical sector.

In this vein, interest was building in a European regulatory authority for medicines, under which the two Community authorization procedures could be subsumed. This eventually came to pass with the launch of the European Agency for the Evaluation of Medicinal Products (EMA) in February 1995. The EMA was established in 1993 via Regulation 2309/93, and was accompanied by legislation which set out a new 'centralized' and 'decentralized' procedure – the former with applications made directly to the agency and the latter a revised form of mutual recognition with the agency arbitrating in the event of disagreements. EMA approvals remain dependent on medicines fulfilling the safety, quality and efficacy criteria laid out in 1965, but the agency was also designed to speed authorizations in the EU, thereby incentivizing

manufacturers. Thus, not just a licensing body for new medicines in the EU<sup>7</sup>, but so too created as an instrument of the single market, the EMEA is perhaps the clearest example of the post-1992 industrial policy direction of EU pharmaceutical policy.

This single market leaning within the EMEA, and EU pharmaceutical policy more widely, has since continued. A review of the EU legislation in 2004 has seen important adjustments made to the agency's mandate – in terms of improving both its public health and industrial policy functions – but gaps remain and not all the changes are completely defined (MiEF 2004). In this way the Commission's approach to pharmaceutical policy remains focused on serving the needs of Europe's pharmaceutical industry and fulfilling the requirements of the single European market, while at the same time stressing a strict health protection role within that. We see this in more recent legislation pertaining to clinical trials (Directive 2001/20/EC), proposed pediatric medicines legislation (COM 2004 599 final) and in the adjustments made to data exclusivity rights within the 2004 review legislation itself. This is not to downplay the Commission's or other EU policy-makers' commitment to public health in pharmaceutical policy, but to highlight that the public health origins of the regulatory regime have since been overtaken by single market and industrial policy concerns. The fact remains that the regulation of medicines within the EU is a shared EU-member state function, and the constitutional asymmetry within EU policy generally, exacerbates the EU's lack of a healthcare policy role. As such, the Commission has sought to make pharmaceutical policy where and when it could, and most policy has been aimed at trying to bring the pharmaceutical sector in line with the single market.

#### **4.3.2 The medical device sector**

What are medical devices? In EU law, a medical device is *not* an organ, not a prescription drug, not a transplant, not a human tissue-engineered product, nor a blood product or a cosmetics. A medical device is everything else that is used in clinical practice, research, laboratory testing and patient care. This means a massive number of

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<sup>7</sup> This gives the EMEA a quasi-regulatory function which can be compared to the information disseminating and guideline issuing mandates of the other EU agencies.

heterogeneous products. Medical device vigilance was mandated by the IVDD directive in 1998 amending the previous directives, and thus entirely blurring the lines between trade and health aspects. Fifteen years after its first involvement in three medical device-specific directives – the AIMD of 1990, the MDD of 1993 and the IVDD of 1998 – in 2005 the Commission proposed new draft rules for a fourth directive to support cell or tissue-based therapies.<sup>8</sup> The objective of drafting these four directives and other rules is to enhance EU-wide regulatory capacity at the same time as avoiding the rise of divergent national approaches. The draft fourth directive aims to create a stand-alone “single, integrated and tailored European regulatory framework” for advanced therapies (all gene, cell or tissue based therapies)<sup>9</sup>, thus completing a regulatory framework specific to medical devices. As the draft states:

[I]n accordance with the subsidiary principle, the proposal fully respects national competence as regards the use or non-use, for ethical reasons, of certain types of human cells (e.g. germ cells or embryonic stem cells). Decisions on such use or non-use remain a national responsibility. The Commission is of the opinion that human tissues and cell-based products should be founded on the philosophy of voluntary and unpaid donation, anonymity of both donor and recipient, altruism of the donor and solidarity between donor and recipient.<sup>10</sup>

Rather than a fully unified EU regulatory approach for all four directives on medical devices, we discover not only legal, institutional and procedural variations within the medical device-specific framework, but also across the two sectors.

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<sup>8</sup> “A human tissue-engineered product (hTEP) means any autologous and allogeneic product which:

- contains, consists of, or results in engineered human cells or tissues; and
- has properties for, or is presented as having properties for, the regeneration, repair or replacement of tissue, where the new tissue or cells, in whole or in part, are structurally and functionally analogous to the original tissue that is being regenerated, repaired or replaced.

Engineered means any process whereby human cells or tissues have been substantially Manipulated, so that their normal/specific physiological functions have been attained.

Human tissue-engineered products are derived from living cells or tissues, with the final product containing viable or non-viable cells. They may, for their function, also contain cellular products, bio-molecules and biomaterials (including chemical substances, scaffolds and matrices)” (Bock et al 2005:14).

<sup>9</sup> <http://europa.eu.int/rapid/press/ReleasesAction> (accessed 11/28/2005).

<sup>10</sup> <http://pharmacos.eudra.org/F2/advtherapies/index.htm> (accessed 11/28/05).

Unlike the approach taken in the first three directives, the Commission (after wide consultation with an array of interested parties) is now proposing a ‘centralized marketing authorization procedure’ similar to pharmaceuticals. The intention is to set up a new expert Committee within the EMEA, to develop tailor-made technical requirements adapted to the particular characteristics of these highly sensitive products; to strengthen the requirements for risk management and traceability as well as to require top quality scientific advice and, lastly, to provide special incentives for small and medium-sized enterprises. These measures definitely move the regulation of human cells considerably closer to the pharmaceutical regime in much the same way as the approach to in-vitro diagnostics taken by the 1998 IVDD – which amended the previous directives – were a first step away from the initial regulatory measures enacted in the early 1990s. There was considerable disagreement between the Commission and national regulators, as well as differences among the member states. Representatives of the pharmaceutical and medical device industries also expressed differing opinions. The key issue was whether medical device regulation should be added to the pharmaceutical regulatory framework? Or, conversely, whether a distinct medical device regime ought to be developed on the grounds that there is no ‘one-size-fits all’ mode of regulation? Fifteen years later, and after long series of conflicts and debates, there is now a widespread consensus that the earlier approach to medical device regulation (1990, respectively 1993) were too lax.

The strategy for a specific ‘medical device regime’ was successfully pursued by the industrial stakeholders in alliance with the Commission, and supported by national governments. Whether national regulators or the industry were the main lobbyists for such a regime does not need to be settled, although it was probably was both. The process to approval was not as smooth as some had hoped for; concerns for patient safety and public health were sorely missing in all the regulatory provisions surrounding conformity assessment procedures, ERs and standards, etc. Yet, over time, the same set of stakeholders who supported the initial step away from the existing EU pharmaceutical regime began to be more open to debates on patient safety and public health. After the adoption of the IVDD in 1998, regulation was no longer exclusively framed as a trade issue; it was acknowledged that devices were able to be regulated on the grounds of being

immediately relevant to patient safety and public health as well. Under pressure from the European Parliament, and thanks to the persuasiveness of the arguments that the promoters of stricter rules advanced, national regulators thus supported a progressive move away from an exclusive trade-orientation (incorporated in the first two directives of 1990 (AIMDD) and 1993 (MDD)).

The move away from the medical device regulatory regime (reflected in the AIMD and the MDD) was made possible by a change in politics among the interested parties, input from regulatory science, as well as a learning curve among all participants in the process about the sensitive nature of tissue-engineered devices and advanced therapies (gene therapy and somatic cell therapy). The relationship between regulatory science and politics in this area has thus come full circle since about 2002. The Commission was leading the on-going debates and launched several consultations in 2002, 2004 and 2005, which ended with the suggestion neither to cover these products under the medical device regime nor under the pharmaceutical regime without developing product-specific regulatory requirements to be administered by EMEA and significantly amplified and expanded for advanced therapies and human tissue engineered products. A consensus has been emerging by mid-2005 that a stand alone regulatory framework for these new products is best. Whether this will hold remains to be seen when the final draft will be before the Council and the European Parliament.

According to the Commission's Consultation paper (2005) gene therapy and somatic cell therapy is already applied in clinical practice for the treatment of various inherited diseases, cancer, diabetes, Parkinson's disease and other neurodegenerative disorders. The importance of human tissue engineering lies in that it helps to regenerate, repair or replace diseased tissues. Unlike the previous AIMD, MDD and IVDD, these three types of new products would come under the Community-wide pharmaceutical regime, and EMEA – the EU-level enforcement agency for the centralized procedure for pharmaceutical market licensing – would receive expanded powers over these new products. All borderline products are now subject to the Community-wide pharmaceutical regime; and for products used in 'regenerative medicine' a product-by-

product risk management would replace risk management by classifications of categories of medical devices. The 2005 draft is written in the form of a Regulation and takes direct effect on regulatory targets (unlike directives which require transposition into national law).

The organization of the authorization of hTEPs products in the member states varies greatly ranging from no classification of hTEPs in some countries (Ireland and Netherlands only require an import license), to their classification as medicinal products (Austria, Germany, Finland and Belgium, to a case-by-case approach classifying them as medical device or pharmaceutical (Spain, UK and Sweden). In France, Spain and Belgium tissue banks play an important role (Bock et al 2005).

## **5. Summary**

This comparison of EU pharmaceutical and medical device regulation, as yet work in progress, has yielded several insights which bear highlighting. Both sectors are exposed to similar EU interventions according to Treaty-based competencies and ECJ court rulings. The policy environment in which they operate, particularly in regard of issues relating to market access, international trade and regulatory convergence, and the competitiveness of the industry, is similar. Both are directly impacted upon – indeed their regulatory policy direction is in large part shaped by – the free movement and harmonization requirements of the single European market. In that way they are significantly affected by an imbalance in priorities between trade and public health competencies and priorities at supranational level. EU regulatory policy-making for the two sectors is thus characterized by a considerable degree of shared responsibility between the EU and the member states. Moreover, this is the case at each phase of the regulatory life cycle. The ‘clash’ between the supranational free movement rules (the driving force of industrial policy) and national health policy competencies, and the ‘paradox’ of EU regulation and the CE marking system, also remain intact. At the same time, both represent independent and nuanced regulatory regimes, stemming from the timing of their respective launches and the wider European context each was subject to

(whether institutional, political or even in terms of member state relations). It remains to be seen whether any (further) convergence between the two is likely to take place, or whether – as representatives of each sector are often keen to point out – the two industries and sectors are manifestly distinct from one another, and should be treated as such.

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York: Oxford University Press.

**Table 1: Interface of Industrial Policy with Healthcare and Public Health Policy**

Product Type	Healthcare Policy	Industrial Policy	Public Health Policy
Drugs	Cost-containment and improving efficiency in healthcare services and care	Promote local research and development	Safe medicines
Medical Devices	Cost-containment and improving efficiency using devices in medical-surgical procedures, assisting patients, and improving the efficiency of in vitro diagnostic tests	Same as above	Safe, high quality, well-performing and efficacious medical devices classified by risks
Drugs	Cost-effective medication	Intellectual property	High quality preparations
Medical Devices	Cost-effective medical-surgical procedures and diagnostic tests	Protection of property rights in some countries; special status on patenting in the EU	High quality devices performing throughout the life cycle of the product; high quality and reliable <i>in vitro</i> diagnostics
Drugs	Regulating doctor and consumer behavior <i>vis-à-vis</i> medicines	Supporting local scientific community	Efficacious treatment
Medical Devices	Regulating doctor and consumer behavior <i>vis-à-vis</i> medical devices	Same as above	Efficacious medical-surgical procedures and reliable tests
Drugs	Generic promotion and/or substitution	Generating and protecting employment	Innovative cures
Medical Devices	Substituting medical devices for pharmaceutical treatment and <i>vice-versa</i> ;	Same as above	'Breakthrough' innovations, alternative treatments, and reliable diagnostic tests
Drugs	Improving prescribing	Promoting small and medium enterprises	Patient access to medicines
Medical Devices	Improving the use of medical devices and diagnostic tests	Same as above	Patient access to innovative medical surgical procedures, diagnostic tests and patient-assisting devices
Drugs	Ensuring access to medicines	Contributing to positive trade balance	
Medical Devices	Ensuring access to innovative procedures and tests	Same as above	Safe use of medical devices and maintenance
Drugs		Sustaining the university research base	
Medical Devices	Improving clinical outcomes	Same as above	Improving health and patient safety

Comment:  
Comment:

Source for pharmaceuticals: Permanand (2006); source for medical devices Altenstetter (XXX). No priority ranking is intended.

**Table 2 : National Actors and Policy Objectives in the Pharmaceutical Sector**

<b>SECTOR</b>	<b>ENTITY</b>	<b>POLICY OBJECTIVES</b>
<b>STATE</b> regulation funding delivery economic	<i>Ministries</i> health finance service trade, industry	<ul style="list-style-type: none"> <li>• adequate supply of safe, quality and effective medicines</li> <li>• minimize tax-funded health expenditure</li> <li>• maximize access to care for those most in need</li> <li>• encourage local industry, employment and exports</li> </ul>
<b>INDUSTRY</b> innovation reproduction distribution insurance	<i>Firms</i> research generic wholesalers insurers	<ul style="list-style-type: none"> <li>• maximize profits and safeguard research base</li> <li>• improve competitive position</li> <li>• improve margins</li> <li>• segment market to best advantage</li> </ul>
<b>PROFESSIONS</b> prescribing dispensing	<i>Associations</i> medicine pharmacy	<ul style="list-style-type: none"> <li>• maximize autonomy and meet patient needs</li> <li>• enlarge professional role and meet client needs</li> </ul>
<b>HEALTH SERVICE</b> primary secondary regional	<i>Organizations</i> practices hospitals health systems	<ul style="list-style-type: none"> <li>• maintain local visibility and community support</li> <li>• maintain market share and organizational visibility</li> <li>• meet requirements of key stakeholders</li> </ul>
<b>OTHER</b> consumers scientific community media	<i>Various</i> associations/patient groups journals firms	<ul style="list-style-type: none"> <li>• ensure access to safe and effective drugs</li> <li>• advance knowledge and academic freedom</li> <li>• enhance or maintain market segment</li> </ul>

Source: adapted from Davis (1997: 21)

**Table 3: Synoptic Timeline of EU Pharmaceutical and Medical Device Regulation**

	<b>Pharmaceuticals</b>	<b>Medical Devices</b>
1960s	In the aftermath of the Thalidomide tragedy it becomes clear that both national and European level controls on medicines, in the interests of patient safety, is required. The European Community agrees its first pharmaceutical-specific legislation in 1965, which defines what a medicinal product is, and sets out safety, quality and efficacy as the criteria for approving new medicines	
1970s	With closer economic and trade relations between EC member states developing at a rapid pace, a Community mutual recognition procedure for new medicines and centralized medicines committee are agreed. The procedure fails to attract sufficient interest from the industry, and the member states remain unsure, such that manufacturers continue to apply directly to national markets.	
1980s	Member states continue to query each others assessments under the mutual recognition procedure, leading to its reform (now the multi-state procedure). The procedure remains unpopular with the member states, and the industry is skeptical because of fears of delays. With pressure developing in the run up to the single market, European policy-makers begin to talk of an agency and introduce a procedure specific to biotechnology products. In order to meet the free movement imperatives of the single market – as laid out in the Single European Act – a raft of legal instruments on a host of issues including advertising, package labeling, etc are introduced in the late 1980s, and discussions regarding an agency are now openly progressing.	Before 1990 regulation only in France, Germany, the UK and the USA; focus on safety of machines over the safety of implants and quality products; no concern for medical vigilance as understood later in EU regulation

1990s	<p>Safety, quality and efficacy remain at the sole approval criteria for new medicines, and in 1993 legislation on the establishment of a European Agency for the Evaluation of Medicinal Products is agreed. The EMEA is launched in 1995, absorbing and reforming the earlier procedures, and strict timelines are set in place for the approval or rejection of new medicine applications. The agency is a unique regulatory body in the EU, but begins to attract criticism for working too closely with, and on behalf of, industry and industrial policy interests rather than public health interests.</p>	<p>1990: Active Implantable Medical Device Directive (effective in member states on January 1, 1993)  1993: Medical Device Directive (effective in member states on January 1, 1995)  Emphasis on quality, safety and performance; efficacy and clinical outcomes are of concern to the 1998 Directive.  1998: In-Vitro Diagnostic Directive (effective in member states June 7, 2000, with transition periods until 2003, respectively 2005--amends the previous directives, tightens regulatory requirements--increases authority of Competent Authorities to monitor notified bodies--creates an EU databank: EUDAMED with two innovations: increases regulatory authority of notified bodies for CE-marking and informing others about CE-certificates issued, modified, supplemented, suspended, withdrawn or refused*--introduces health-monitoring measures to be applied by healthcare providers.</p>
2002 onwards	<p>A review of EU pharmaceutical legislation is completed in 2004. It makes changes to the structure and mandate of the EMEA, inter alia: permitting the quicker approval for products of major therapeutic interest or early approval in the case of a public health emergency; stricter transparency requirements for drug applications and information, a widening of the scope of products qualifying for centralized approval. Discussion on other EU pharmaceutical policies e.g. for pediatric medicines or clinical trials, are at advanced stages or awaiting implementation by the member states.</p>	<p>Commission-led consultations on a draft regulation on human tissue-engineered products (hTEP) and advanced therapies--new expert committee within EMEA--yet stand alone regulatory framework and respect for home country control or subsidiary.</p>

\* There are no publicly available statistics on the activities of notified bodies.

**Table: 4 Differences in the Nature of Drugs and Medical Devices**

Medical Devices	Pharmaceutical Products
<ul style="list-style-type: none"> <li>Industry is made up of a few large companies and a large number of very small companies; the industry is extremely diverse and fragmented</li> </ul>	<ul style="list-style-type: none"> <li>Industry has undergone considerable consolidation and is dominated by a few multinationals</li> </ul>
<ul style="list-style-type: none"> <li>Traditionally based on mechanical, electrical and materials engineering</li> </ul>	<ul style="list-style-type: none"> <li>Traditionally based on pharmacology and chemistry; they typically are absorbed, distributed, metabolized, excreted</li> </ul>
<ul style="list-style-type: none"> <li>Products engineered to perform certain functions based on specific performance and safety requirements; the therapeutic effect can in many cases be patient triggered or automatically adapted to the patient condition</li> </ul>	<ul style="list-style-type: none"> <li>Product development by trial on active substances selected on the basis of safety and efficacy</li> </ul>
<ul style="list-style-type: none"> <li>Effective by mechanical and/or electrical action; mainly pharmacologically inactive</li> </ul>	<ul style="list-style-type: none"> <li>Pharmacologically active; effective when absorbed into the human body</li> </ul>
<ul style="list-style-type: none"> <li>Recent regulations: part of the European “New Approach”</li> <li>CE Marking ensures product conformity with Essential Requirements*</li> <li>Assessment, controls and requirements increase in proportion to potential risk, the highest level requiring design and clinical evaluation</li> <li>Notified Bodies are appointed by the governments to certify the conformity assessment procedures</li> </ul>	<ul style="list-style-type: none"> <li>Long established prescriptive EU legislation</li> <li>Legislation based on pre-market approval/licensing</li> <li>All pharmaceutical products are subject to product approval</li> <li>Pharmaceuticals are registered either centrally via EMEA (European Medicines Evaluation Agency) or the Member States (decentralized procedure); this involves clinical trials involving thousands of people</li> </ul>
<ul style="list-style-type: none"> <li>Continuous innovation based on new science, technology and available materials</li> </ul>	<ul style="list-style-type: none"> <li>Continuous innovation and some improvements based on new science and technology; discovery of active substances with long term evaluation to determine effects and side-effects</li> </ul>
<ul style="list-style-type: none"> <li>Short product life cycle due to continuous incremental improvements; often user related/driven</li> <li>Short amortization period</li> <li>More stringent patient-specific traceability is imposed to track long-term effects of implants</li> </ul>	<ul style="list-style-type: none"> <li>Extensive product life cycle with prescription-only often moving to OTC allowing for:</li> <li>Long amortization period</li> </ul>

\* Essential requirements are outlined for chemical, physical, and biological properties, infection and microbial contamination; construction and environmental properties; devices with measuring function; protection against radiation; requirements for medical devices connected to or equipped with an energy source (including electromagnetic compatibility); and information to be supplied by the manufacturer.  
Source: EUCOMED (2003: 60).