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Robert Kaiser  
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**Germany's Role in Global Pharmaceutical Regulation:  
The Europeanization of Interest Mediation and Institutional Dynamics in an  
Extended Multi-level Governance System**

By

**Robert Kaiser**

**Abstract**

Since the 1990s, the member states of the European Union (EU) have in an increasing number of cases agreed to pool their individual market power in order to valorize their bargaining position in various global governance arrangements. The most prominent examples of those interactions with multilateral regimes certainly are the World Trade Organization and the global climate regime. Against this background, this paper has a theoretical and an empirical aim. Concerning the theoretical perspective, the paper proposes an extended multi-level governance approach (eMLG) in order to analyze the dynamics of institutional change that emerge both at the EU and the member states' level as a consequence of the agreement to Europeanize the mediation of national interests. Empirically, I refer to the example of global pharmaceutical regulation and I ask why even larger member states of the EU, such as Germany, engage in the Europeanization of interest mediation and under what conditions they are able to pursue their interests if the European Commission represents them at the global stage. In this respect I argue that not the size or the relative power of individual member states play a decisive role, but their ability to make use of the institutional multi-level structure.

**About the Author**

**Robert Kaiser** (Ph.D. from the University of Dusseldorf, 1997, Habilitation from the University of Munich, 2006) is Acting Chair for Governmental Studies at the University of Hamburg. His main fields of research are processes of Europeanization and institutional change in innovation, environmental and trade policies. He is the author of *Innovationspolitik: Staatliche Steuerungskapazitäten beim Aufbau wissensbasierter Industrien im internationalen Vergleich* (Baden-Baden: Nomos, 2008) and the Co-Author of "The Reconfiguration of National Innovation Systems" (*Research Policy* (2004) 33), "Managing Diversity in a System of Multi-level Governance" (*Journal of European Public Policy* (2004) 11), and "Missing the Lisbon Target? Multi-level Innovation Systems and the Challenge for EU Policy Coordination" (*Journal of Public Policy* (2005) 25).

## **Contact Information**

PD Dr. Robert Kaiser, Institute for Political Science, University of Hamburg,  
Allendeplatz 1, D-20146 Hamburg; E-Mail: [mail@robert-kaiser.de](mailto:mail@robert-kaiser.de), Homepage:  
[www.robert-kaiser.de](http://www.robert-kaiser.de).

## Preface

This paper was presented during a conference on 'Germany in Global Economic Governance', which took place at Cornell University on Feb. 22/23, 2008. It was organized by Stefan Schirm (Ruhr University of Bochum) and Hubert Zimmermann (Cornell). We would like to thank our sponsors, the DAAD (German Academic Exchange Service), the Department of Government, the University of Bochum, the Mario Einaudi Center for International Studies, the Institute for European Studies as well as Peter Katzenstein (Cornell), who served as commentator.

Germany, still the third or fourth largest global economy, has been particularly active in proposing a tighter regulation of international financial markets. We use Germany as an exemplary case of how medium-sized countries can shape global governance and how the political economy of countries with coordinated market economies conditions their global governance strategies as compared to so-called liberal market economies, such as the United States and the United Kingdom. With this focus, the project permits and initiates an overdue dialogue between the literatures on varieties of capitalism and on global governance, using global governance as the dependent variable. Another objective of the workshop was to address the dearth of country-specific case studies in research on global governance which often treats all states as essentially similar in their reaction to economic globalization.

Contributors were asked to look at various areas of global governance (such as hedge fund regulation, IMF reform, Basel II, pharmaceutical regulation, corporate governance, transgovernmental standard-setting, etc). All papers identified several levels shaping the German position: the subnational, the European and the global level. The German government, with varying success, engaged in strategic forum-shopping among these levels. A further characteristic was close cooperation between state and non-state actors. Overall, the extent of Germany's capacity to shape global governance is surprisingly large.



## **Germany's Role in Global Pharmaceutical Regulation: The Europeanization of Interest Mediation and Institutional Dynamics in an Extended Multi-level Governance System**

### **Introduction: The Emergence of a Global Regime for Pharmaceutical Regulation<sup>1</sup>**

During the last three decades hardly any industrial sector has been affected by such a fundamental technological paradigm shift as it has occurred in the pharmaceutical industry. Today new biomedical technologies allow for, at least in principle, a process of rational drug design, which has overturned the fundamental logic of “trial and error” on which traditional pharmaceutical development processes were based. This paradigm shift from chemistry-driven to genomics-based drug development had many consequences (Grande/Kaiser 2006; Kaiser 2008a). The most important one certainly was that pharmaceutical companies became confronted with severe productivity and innovation problems. Although the expenditures for research and development have increased dramatically - those of the U.S. pharmaceutical industry, for example, have multiplied tenfold between 1980 and 2001 - the number of market authorizations for new chemical entities has sharply decreased. As a consequence, mainly in the 1980s and 1990s pharmaceutical firms felt impelled to join forces and thus set off a wave of cross-border mergers and acquisitions within this industry.

In parallel, governments in most industrialized countries have also reacted to these developments by the means of increasing public spending for biomedical research and the de- and re-regulation of the pharmaceutical development process. With respect to public spending, the U.S. National Institute of Health (NIH) boosted its annual budget for extramural research to more than 20 billion USD while the German federal government in the early 1990s started to invest some 750 million EUR per year into the establishment of a modern biotechnology industry (Kaiser 2008b: 21). In the United States, regulatory agencies came under increasing pressure, both from pharmaceutical companies as well as

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<sup>1</sup> An earlier version of this paper was presented at the workshop “Germany in Global Economic Governance” at Cornell University, February 22, 2008. I would like to thank Peter J. Katzenstein, Daniel Kinderman, Andreas Nölke, Stefan A. Schirm, and Hubert Zimmermann for valuable comments.

from patient interest groups to deregulate the process of market authorization in order to bring innovative pharmaceuticals faster to the market. In the European Union, regulatory procedures for modern biopharmaceuticals were centralized in the mid-1990s thus providing for a single marketing authorization for the common market.

In this context it served the interests of both pharmaceutical companies and governments to go a step further and to initiate a process of harmonization of pharmaceutical regulations at the global level. From a corporate view, the increasing costs for pharmaceutical innovations have a less serious impact if testing procedures for chemical entities are highly standardized on all major pharmaceutical markets. This especially holds because more than fifty percent of the overall costs for the development of a pharmaceutical product are directly related to clinical trials. Harmonization therefore significantly reduces the financial burden of pharmaceutical companies if clinical trials that were done and documented on the basis of common standards in one specific country would be widely acknowledged in others.

Nation-states and their governments, however, have different reasons to perceive the global harmonization of pharmaceutical regulation as beneficial. This is mainly due to significant shifts of market shares that have occurred during the last decades. Germany, for example, enjoyed a reputation as “the pharmacy of the World” for the most part of the twentieth century with constant World market shares of about 40 percent. Since the 1970s, however, this market share has fallen gradually to 8 percent and has been further on cut to half during the 1990s.

Therefore, from a German perspective the global harmonization of regulatory standards would primarily compensate for a shrinking home market as it might also improve the country’s competitive position on the market for clinical trials. The United States, in contrast, today represents a global market share of almost 50 percent. In this situation better access to international markets is not per se a strong argument for international cooperation. Given the fact, however, that the U.S. is also one of the very few countries in the World that has by far and large not implemented yet price controls on



pharmaceutical products, the country's health system is confronted with a situation in which domestic pharmaceutical companies are able, if not to some extent forced, to re-finance their R&D investments mainly at the home market. Faster access to foreign markets would therefore at least to some extent relieve the U.S. health system from these costs.

The kind of institutional arrangement that was chosen in 1990 when the "International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use" (ICH) was established certainly reflected the common interests of companies and governments in the leading pharmaceutical markets. The ICH was set up as a consensus-driven trilateral initiative, comprised of representatives from regulatory agencies and pharmaceutical industry organizations from Europe, Japan and the United States. As such it was able to build upon a series of bilateral mutual recognition agreements that had been concluded earlier among these countries, which had in 2003 a combined World market share in pharmaceutical products of almost 90 percent. Even though the ICH from the beginning invited regulatory agencies from other countries to become observers to this new organization, priorities for harmonization and methods of implementation have been clearly defined within the trilateral context.

This paper aims at answering two questions that are closely related to the assessment of Germany's current role in global pharmaceutical regulation. The first question is why even larger EU member states, such as Germany, agreed to Europeanize the mediation of national interests in this field. From what has been said already it is obvious that the German government may strengthen its position in multilateral arenas by pooling its individual pharmaceutical market power with other European countries that together have an aggregated World market share of roughly 30 percent. This argument alone is, however, not sufficient. This is mainly because of the fact that the Europeanization of the mediation of interests takes place within a specific institutional structure, which can be characterized best as an extended system of multi-level governance (eMLG). Therefore, the second question raised in this paper is under what conditions EU member states are able to pursue their interests in such an institutional structure. In this respect I argue that

not the size or the relative power of individual member states play a decisive role, but their ability to make use of the institutional multi-level structure. As a consequence, the member states' influence on the Global regime for pharmaceutical regulation largely depends on their ability to adapt their domestic regulatory system to the institutional structure that has been established at the European level.

In order to develop this argument the next section will firstly identify the four specific reasons why it was rational for the EU member states to delegate the task of representation within the ICH to the European Commission and thus initiated the establishment of an extended multi-level governance system even in this policy area. Subsequently, section 3 will turn to the three institutional characteristics of this multi-level system. Here it will be firstly shown that the delegation of representation took place only under the condition of ongoing tight control of the EU Commission's activities exercised by the member states' governments. Moreover, even the Europeanization of interest mediation does not necessarily mean that European institutions are in full charge of the representation of the European Union. Rather, the European scientific representatives within ICH committees are in fact national experts who participate on behalf of the European regulatory agency for pharmaceutical products (EMA) that has to rely on national expertise since its own resources are extraordinarily limited compared to regulatory agencies in Japan or the United States. Secondly, within this extended multi-level governance system the supranational legal system of the European Union provides for the opportunity to transform globally agreed soft-law into compulsory Community hard-law and therefore guarantees not only a certain degree of harmonization within the EU, but also compliance with ICH recommendations toward third countries. And thirdly, the extended multi-level governance system induces considerable pressure on the member states to evaluate the performance of their domestic regulatory systems. Section 4 will expatiate on this point and will provide the crucial empirical evidence for the claim that the institutional structure of the eMLG system creates a retroactive pressure for institutional reforms at the national level. In more concrete terms, there has been increasing pressure on the member states to adapt to a new "superior" regulatory model

in order to maintain influence on European and Global processes of pharmaceutical regulation. Finally, section five will summarize the main theoretical and empirical conclusions.

### **The National Rationale for the Europeanization of Interest Mediation in Global Pharmaceutical Regulation**

There are basically four interdependent reasons why EU member states agreed at the end of the 1980s to pool their market power and mediate their interests in global pharmaceutical regulation at the European level.

The first reason can be seen in the attempt of the European Union to substantiate its own ambitions to establish a European single market for pharmaceutical products with a related global initiative. In fact, it was the European Commission that proposed such an initiative at the end of the 1980s in a number of bilateral discussions with regulatory agencies in Japan and the United States. These bilateral discussions materialized in a plan of action agreed upon at the WHO Conference of Drug Regulatory Agencies (ICDRA) in Paris in 1989. The formal establishment of the ICH followed only a few months later (April 1990) at a meeting hosted by the European Federation of Pharmaceutical Industries' Associations (EFPIA) in Brussels. Therefore, the ICH initiative as well as the establishment of a common European approach towards drug regulation took place at the same time. Only in 1987, the European Council decided to end a cumbersome and less effective process of mutual recognition of national drug approvals that was initiated already in 1963 (Vogel 1998). A new centralized approach towards the harmonization of market authorization procedures for novel biopharmaceutical drugs thus paved the way for the establishment of the European Medicines Agency (EMA) in 1995. This turn towards positive, market shaping, integration at the European level certainly was a central precondition for the ICH process.

Traditionally, countries that have a significant pharmaceutical industry dealt with the problem of trans-border trade in pharmaceutical products by the conclusion of Mutual Recognition Agreements (MRAs) or Memoranda of Understanding (MOUs) between the

competent regulatory agencies that provided both for the general acceptance of other countries' regulatory frameworks for the testing and production of pharmaceuticals, but also for the inspection of foreign production facilities. The existence of these agreements was and still is an important precondition for the liberalization of trade in pharmaceutical products, which accelerated in course of an agreement on the elimination of customs duties reached by 23 countries during the Uruguay Round of the General Agreement on Tariffs and Trade (GATT). Both MRAs and MOUs are, however, mainly concerned with the issues of public safety and consumer protection. They are typical tools of negative integration in the sense that they have a market-making character while reducing the states' capacities to control the quality and security of foreign products on the home market.<sup>2</sup> Positive integration, in contrast, not only aims at common standards for the development and production of pharmaceuticals it also tackles the problem of faster access to markets for and better supply with novel innovative drugs. Against this background, the ICH effort to harmonize respective regulations also is a process of market-shaping positive integration by which national regulatory agencies regain control over the methods and standards for the production of pharmaceuticals outside their own jurisdiction (Scharpf 1996).

A second reason for the delegation of representation in pharmaceutical regulation certainly is that the EU, representing a population of more than 500 million people, accumulates a substantial economic weight that provides for the opportunity to export internal standards to the outside World. This means that the pure size of the market compensates for the relatively weak position in which the European member states are in terms of their respective pharmaceutical industries. Although seven of the 20 largest pharmaceutical companies in the World are based within the European Union, in 2002

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<sup>2</sup> Even the capacities of the U.S. Federal Food and Drug Administration provide only on a rather limited scale for conducting inspections of foreign production facilities that produce pharmaceuticals that are exported to the United States. See "Testimony on the Agreement on Mutual Recognition between the United States and the European Community by Sharon Smith Holston Deputy Commissioner for External Affairs, Food and Drug Administration Before the House Committee on Commerce, Subcommittee on Oversight and Investigations October 2, 1998.

those companies had an aggregated World market share of only 20 percent. European pharmaceutical companies contributed only two pharmaceutical products to the list of the 10 top-selling drugs. Moreover, they hardly play any role on the Japanese market, which is the second largest national market in the World. In terms of market sales only two companies are ranked (on 13<sup>th</sup> and 14<sup>th</sup> position) on the list of the 20 leading companies.

Therefore it is not the strength of the industrial base, but the existence of harmonized rules and regulations for the access to 27 national pharmaceutical markets that provides the EU Commission with a significant amount of negotiation power in Global arrangements for pharmaceutical regulation. With respect to the ICH harmonization process it has been argued that the European Union “has found it the easiest to adjust to the ICH guidelines”, because “most guidelines largely overlap with current EC legislation” (Vogel 1998: 14). This shows that the Europeanization of pharmaceutical regulation made it possible that the EU member states successfully pursued their collective interests. And even beyond the topic of pharmaceutical regulation there are indications that the European Union increased its influence in Global standardization processes. The judgment that the EU is becoming the world’s chief regulator (The Economist, September 20, 2007) might be a little bit premature. Nevertheless, there is of course a competition in many fields between the U.S. cost-benefit approach toward regulation and the emphasis of the precautionary principle that guides European regulation.

A third reason for the mediation of interests at the European level is that the Europeanization of pharmaceutical regulation strengthens the coherence between the different EU external policies. This is because the ICH is embedded in a broader network of international and regional organizations, such as the World Health Organization (WHO), the World Trade Organization (WTO) or the European Free Trade Association (EFTA), as well as of other national regulatory agencies and private actors who have become observers to the ICH process. Given this, the ICH is a typical example of global economic governance defined as a multilateral and rule-based management system for the steering of the World economy (Schirm 2004: 237). In this context, ICH guidelines do

not only provide for common standards among participating parties, they also lower the risk for member states to violate the rules of the Agreement on Technical Barriers to Trade (TBT) since the WTO, as an organization that imports standards from other international rule-making authorities, explicitly calls upon its member states to adopt those internationally agreed standards (Gstöhl/Kaiser 2004). Therefore, from a European perspective the coherence of EU external policies is likely to increase if the European Commission represents the Union in the various multilateral fora that are concerned with different aspects of pharmaceutical regulation, such as patenting, risk regulation or the prevention from epidemics.

A fourth and final reason for EU member state governments to support the establishment of this extended multi-level governance system for pharmaceutical regulation exists because it facilitates the implementation of new regulatory arrangements at the domestic level. In this respect, Germany constitutes a strong case for the persistence and stability of a tripartistic institutional arrangement comprised of representatives from the Federal Chamber of Physicians (“Bundesärztekammer”), the German Society for Internal Medicine (“Gesellschaft für Innere Medizin”) and the federal health office (“Bundesgesundheitsamt”) as the public authority that granted marketing authorizations. This institutional arrangement can be characterized as a rather “closed shop” of tightly coupled actors who were hardly susceptible to the interests of the pharmaceutical industry as well as of patient interest groups. Outside Germany, in contrast, regulatory agencies both in the United States and in other European countries have reacted to the pressure for a more innovation-oriented regulation by a stronger involvement especially of the pharmaceutical industry.

In the United States, for example, interactions between the FDA and industry have undoubtedly increased since the enactment of the Prescription Drug User Fee Act of 1992, which entitled the FDA to collect substantial application fees from drug manufacturers in order to fund new drug approval processes. In Europe, the EMEA has been explicitly designed as a “service provider” for the pharmaceutical industry. Consequently, the agency acts under the supervision of the Enterprise and Industry

Directorate General of the European Commission and not under the supervision of the unit responsible for health and consumer protection. At the member states' level the British regulatory agency, the Medicines and Health Care Products Regulatory Agency (MHRA), has been widely considered as a role model for an efficient (in terms of the duration of approval procedures) institutional arrangement for pharmaceutical regulation. More recently, however, it has come under enormous political pressure because of the close relationship of some of its employees with the pharmaceutical industry and because of the fact that decisions made by the MHRA were based on insufficient information provided by pharmaceutical companies (House of Commons 2005). Within this context the stability of the tripartistic German regulatory network became precarious both because of its relatively weak performance in dealing with applications for marketing authorizations of novel drugs and because of the competition that has emerged between national regulatory agencies within the extended multi-level governance system.

### **The Institutional Characteristics of the Extended Multi-level Governance System for Pharmaceutical Regulation**

Up to now the concept of an extended system of multi-level governance has not very much advanced neither in theoretical nor in empirical terms. There are only few studies that have analyzed how the international embeddedness of the European Union affects both regulatory processes at the Global level and related policy-making processes within the European sphere. However, there is at least some evidence that the membership of the European Union in the World Trade Organization led to institutional change within the EU. In this respect, it has been shown that the embeddedness of the EU within this international context has not only affected the formal organization of the European decision-making process, but also internal routines, guiding ideas and concepts of legitimate order (Knodt 2004, Billiet 2006). In order to make full use of the concept of an extended multi-level governance system, we also have to dip into different dynamics of institutional adaption at the member states level. This leads to the assumption that an extended multi-level governance system has at least three distinct characteristics that are fundamental to the understanding of these institutional dynamics.

The first feature concerns the rules and procedures that apply to decision-making within the European Union both in regard to internal rules and regulations, but also with respect to the determination of common European positions for negotiations at the Global level. Although we can assume that they differ to some extent across policy fields, we can draw some principle assessments from the literature on multi-level governance in Europe. Hence, a system of multi-level governance reflects “a polity creating process in which authority and policy-making influence are shared across multiple levels of government” (Hooghe and Marks 2001: 2). In this respect, it is widely accepted that the European multi-level polity is characterized both by a dynamic dispersion of authority and a non-hierarchical institutional design (Kaiser/Prange 2002).

This means that decision-making competencies are dispersed across territorial levels, i.e. across supranational, national, and regional or local actors, or allocated sideways, which means e.g. to quasi-autonomous agencies or to non-public implementation bodies (Majone 1996). With regard to aspects of authority relocation it is of special importance that in contrast to federal systems, in a multi-level governance system the interactions between the different levels are not “disciplined” by constitutional norms, which results in a considerable competition for competencies (Grande 2001; Peters and Pierre 2002).

In the case of pharmaceutical regulation the establishment of the EMEA clearly reflects this institutional feature, as this regulatory agency is largely dependent on human and knowledge resources provided by the member states as well as on the confirmation of its recommendations for marketing authorizations by member states’ delegates. Accordingly, the EMEA is still a largely member states and consensus-driven organization. Consensual decision-making is obligatory, for example, in the Committee for Medicinal Products for Human Use (CHMP) where representatives from national regulatory agencies conclude on recommendations for the decision on the market authorization of new drugs. The final “political decision” has to be taken by member states representatives that come together in the European Commission’s Standing Committee on Medicinal Products for Human Use. Here the decisions can be taken by majority voting.



Nevertheless, even in the whole process of drug evaluation the EMEA has to rely mainly on the 47 national agencies that conduct the required procedures and provide the scientific advice for the final decision on market authorization. Even this short description indicates that there are enormous organizational differences between the EMEA and the U.S. Federal Food and Drug Administration, which especially concern the respective resources of the agencies and their dependency on “external” actors. In contrast to the FDA, the EMEA is certainly not a powerful independent regulatory agency. It is better characterized as a hub of a European network of national regulatory agencies. Because of that the actual influence of the different national agencies at the European level is largely dependent on their respective scientific expertise and their capabilities in the process of evaluating new pharmaceutical products.

**Table 1: Comparison of organizational features of the EMEA and the FDA<sup>3</sup>**

	EMEA	FDA
Established in	1995	1931
Budget for 2001	EUR 62 million (of which 70 percent originated from the pharmaceutical industry)	EUR 1,450 million (of which 10 percent originated from the pharmaceutical Industry and Innovation)
Permanent Staff	250	9,000
Evaluations done by	External experts (each member state appoints two of them)	Internal Staff (with advice from external experts)

Whereas the process of granting market authorization for new drugs already reflects the typical non-hierarchical and consensual decision-making structure of the European multi-level governance system, pharmaceutical regulation in Europe seeks not only consensus among member states, but also with industry. In this respect it has been rightly argued that the pharmaceutical industry has an “insider status” within the European Commission

<sup>3</sup> Data for table 1 originate from Garattini/Bertele (2004: 87).

and its various committees that are concerned with pharmaceutical regulation (Permanand/Altenstetter 2004: 42). This holds especially for corporate participation in the High Level Group on Innovation and the Provision of Medicines (called “G10 Medicines”) that was set up by the European Commission in 2000 in order to give policy advice on the various topics of health policy. This group is chaired by the European Commission and comprised of national Health Ministers from seven member states, as well as representatives from the European Parliament, the pharmaceutical industry and patient organizations.

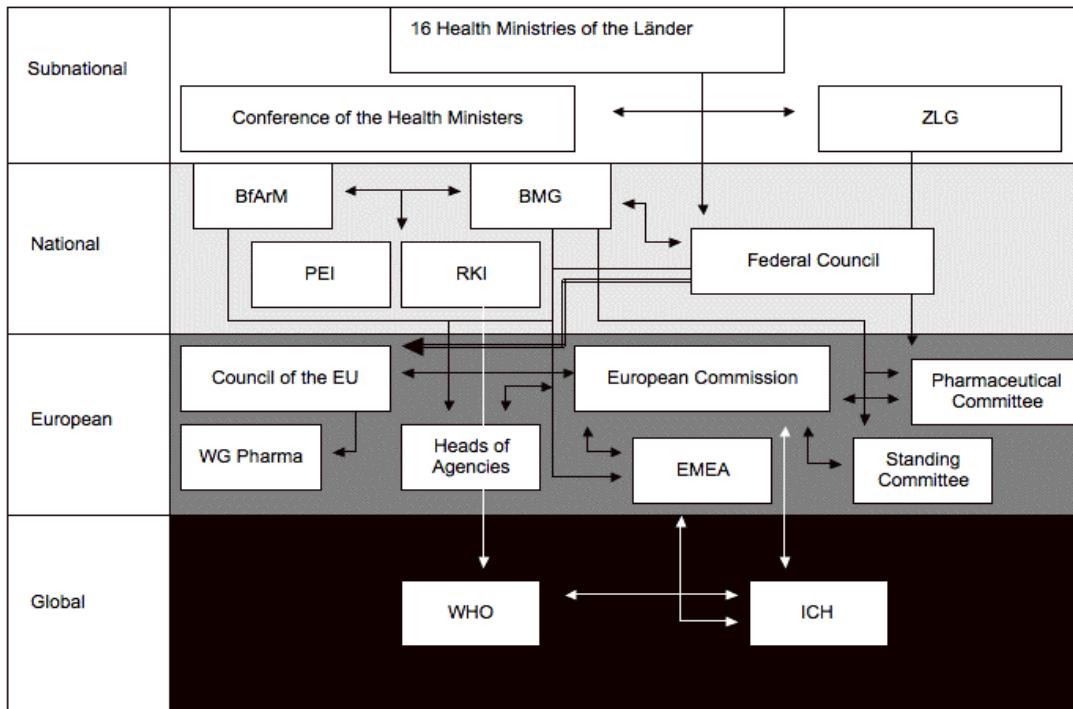
The various feedback loops and co-decision procedures that exist on the one hand between the European Commission, the EMEA and the pharmaceutical industry and, on the other hand, with the member states governments and their regulatory agencies clearly show that within the European polity actors and arenas are not ordered hierarchically, so that “supranational institutions are not hierarchically superimposed upon the member states; and the member states and their regions are not subordinated to the supranational powers” (Grande 2001: 7). Rather, “political arenas are interconnected rather than nested” (Marks et al. 1996: 346f), which means that even subnational actors do not only operate at the national, but also at the supranational levels.

These interactions are also constitutive for the European Union’s participation in the ICH process. Although only the European Union, through the pharmaceutical unit of the European Commission, and the EMEA and its working groups are represented at the ICH the member states have a significant influence on this process.

Accordingly, the member states are able to pursue their interests by using the various channels and arenas that exist within the European system of multi-level governance for pharmaceutical regulation and policy. In this respect, however, the institutional complexity at the European level is not the only difficulty, because the member states differ to some extent in terms of the domestic organization of competences for pharmaceutical regulation.

Therefore, in the German case the high degree of horizontal and vertical differentiation of responsibilities for pharmaceutical regulation is of importance. In the German federal system the authority to grant market authorizations for drugs rests with the federal level if the application has not been made under the centralized European procedure. The German states are responsible, inter alia, for the monitoring of clinical trials, pharmaceutical production processes and the distribution of drugs. They coordinate their activities through the Conference of the Health Ministers of the German states, which convene at least once a year, and the Central Authority of the states for Health Protection with regard to Medicinal Products and Medical Devices (ZLG). The horizontal differentiation at the federal level exists because of the political responsibility of the Federal Ministry of Health (BMG), the responsibility for market authorizations of the Federal Institute for Medicinal Products and Medicinal Devices (BfArM), which is a subordinate authority of the BMG, the Paul-Ehrlich-Institute, a research agency that also operates under the supervision of the BMG, which is responsible for market authorizations of sera, vaccines, blood preparations, and gene transfer medicinal products, and the Robert-Koch-Institute, another research agency of the BMG, that is mainly responsible for the prevention of infections. As a consequence, all actors within the German regulatory system for pharmaceuticals are to a certain extent concerned with regulatory aspects that have been harmonized within the European or the ICH context. In view of the global level, however, German representatives become engaged within the ICH context only as European experts or delegates. That is why it is crucial to understand the degree, the nature, and the dynamics of the national influence at the European level. In this respect, figure 1 provides an overview of the multi-level institutional architecture that exists in pharmaceutical regulation.

**Figure 1: German actors within the extended multi-level system of pharmaceutical regulation**



From a German perspective, the main important actors are the Federal Ministry of Health, which is represented in the Council of the European Union and its Working Group on Pharmaceuticals, in the EMEA, and in the Commission’s pharmaceutical Committee as well as in the Standing Committee on medicinal products for human use. The German pharmaceutical regulatory agency BfArM delegates experts and representatives to EMEA and it is represented in coordination group of the Heads of European regulatory agencies. The German states are engaged in this multi-level structure by sending representatives of the ZLG into the Commission’s pharmaceutical committee (who are officially mandated by the Federal Council) and by comprehensive rights to participate in European legislation (via the Council of Ministers of the EU) that exist for the Federal Council. These participation procedures are of some importance for the process of global pharmaceutical regulation, since ICH guidelines are transformed in Europe into formal legislative directives. Most of them have to be, according to the distribution of powers within the German federal system, implemented by the German states.

In order to evaluate as to how this institutional structure is active in processes of global harmonization of pharmaceutical regulation one has to keep in mind that the EU is represented at ICH level only by the European Commission and EMEA. Within the European Commission, the pharmaceutical unit is responsible for all ICH related activities. However, it has to coordinate its activities with the Pharmaceutical Committee that is comprised of members of national governments (and in the German case even of a representative from the states) and regulatory agencies. This committee meets every six months. In contrast to the European Commission, the EMEA allows for participation of national representatives within the ICH context as delegated experts of EMEA. In this respect, the German regulatory agency (BfArM) has delegated experts in five ICH working groups.

The second institutional feature of this extended multi-level governance system is that it provides for a solution to transform standards and recommendations agreed upon at the Global level into compulsory law within the European polity. This feature is of high importance especially if Global governance arrangements produce, as it is often be the case, non-binding soft law. This process of transformation of soft-law into compulsory Community hard-law is taking place in a number of policy areas in which the European Union has external competences. In the field of health and consumer policy, for example, the EU became a member of the Codex Alimentarius Commission (CAC) in 2003. Since that time, some CAC standards have been introduced into EU legislation in areas such as recommendations concerning microbiological criteria for foodstuffs. In terms of the Global climate regime the EU member states committed themselves to a common EU emission trading system, which is the main tool by which the member states intend to meet their obligations from the Kyoto Protocol.

With respect to ICH recommendations (for details on the specific measures taken by the ICH see Vogel 1998 and Daemrich 2004) it is important to notice that within the European sphere there is a transformation into hard law taking place since the European Commission can use the tool of formal directives to steer the implement these recommendations at the member states level. Within ICH, as in other global governance

arrangements, the legalization by soft law (Shelton 2000) is a superior institutional solution as it is easier to achieve, as it protects the actor's autonomy and as it facilitates compromise "between actors with different interests and values, different time horizons and discount rates, and different degrees of power" (Abbott/Snidal 2000: 423). The critical question is, of course, under which conditions actors will comply with soft regulations.

Generally, compliance with soft regulations should be supported by long-term relationships between actors and their shared belief that these regulations maximize welfare while minimizing transaction costs. Within this extended multi-level system for pharmaceutical regulation long-term relationships are likely to evolve because of the increasing homogeneity of actor constellations that exist at the Global, the European and the national level. We will discuss this aspect in some more detail later in this section.

Since the early 1990s, the process of transformation into hard-law is a rather complex one and can be exemplified by the ICH guidelines on Good Clinical Practice (GCP) agreed upon in 1995. At the European level the EMEA Committee for Proprietary Medicinal Products approved these guidelines in 1996. However, the EU Directive on principles and detailed guidelines for good clinical practice (2001/2005) only required that these guidelines "should be taken into account". Accordingly, the ICH guidelines assumed compulsory character only with the implementation at the member states level. In Germany, for example, the EU directive was implemented in 2006 through the revision of the German Medicinal Products Act, which contains no direct reference to the ICH guidelines. Rather, the German regulatory authorities for pharmaceutical products issued an official notice on the revised law in which they made clear that the requirements for an application for marketing authorization of a medicinal product are generally defined by the CPMP's approved version of the ICH guidelines for clinical trials.<sup>4</sup>

The third institutional feature of this extended multi-level governance system consists of the fact that the degree to which national actors get involved is less determined by formal

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<sup>4</sup> See "Dritte Bekanntmachung zur klinischen Prüfung von Arzneimitteln am Menschen", Bonn: BfArM, 10.08.2006.

rules, but largely depend on their ability to contribute to the performance of the common regulatory system. Accordingly, the degree to which national interests can be pursued in the process of global pharmaceutical regulation largely depends on the capability to make use of the European multi-level policy-making structure. This is mainly because the European Commission and the EMEA need the support and input from the member states in order to negotiate effectively at the global level. This essentially leads to the fact that member states compete with each other for influence and status within the multi-level governance system. Although this institutional feature can explain certain dynamics of institutional change at the member states level, it has been widely ignored by the literature on the European engagement in multilateral governance arrangements. Consequently, the next section will take a closer look on these dynamics.

### **The Retroactive Pressure: Institutional Adjustments at the National Level**

In the field of pharmaceutical regulation, the Europeanization of interest mediation has clearly increased the pressure at least on some member states to adjust their domestic institutional structure to a specific model established both at the European and Global levels. For the German case, this argument is well documented primarily by two developments: firstly, by the federal government's attempt to set up a new independent regulatory agency for the pharmaceutical sector and, secondly, by measures taken by the German states to intensify their coordination in fields of subnational competences.

The German states, for example, agreed on an Inter-state accord, which went into force in 1994, and thereby centralized their competencies in the field of supervision of pharmaceutical production. This initiative was taken as a response to the Europeanization of regulation of pharmaceuticals and medical devices. Therefore, the newly established Central Authority of the states for Health Protection with regard to Medicinal Products and Medical Devices (ZLG) was established as the single national contact point for the European Commission with regard to the safety of medicinal devices and pharmaceutical drugs. Within this context, the ZLG is primarily responsible for the certification of new medicinal products and for the participation in foreign inspections of pharmaceutical

production facilities that take place on the basis on Mutual Recognition Agreements that have been concluded by the European Union. Because of the latter responsibility the ZLG is also a member of the EMEA Ad-hoc Working Group of Inspections Services.

The Europeanization of pharmaceutical regulation made institutional reforms much more inevitable at the national level. Since 1994, the German tripartistic regulatory regime has been dissolved in three main steps. The first step was marked by the reorganization of the federal health office into three independent and specialized agencies of which one, the Federal Institute for Medicinal Products and Medicinal Devices (BfArM) became responsible for the decision on marketing authorizations for new pharmaceutical and medicinal products. In parallel, the Federal Chamber of Physicians and the German Society for Internal Medicine lost their privileged role within the regulatory system, but they maintained some influence as consultants for the BfArM. At first sight, this reorganization was an immediate reaction to a political scandal that arose because of the detection of HIV-contaminated blood bottles. Closer inspection, however, reveals that there had been already before an ongoing discussion about organizational deficits within the federal office, which suffered from a significant increase of responsibilities in various fields of health and environmental protection.

The second step is characterized by a number of political initiatives that were taken during the last decade with the aim of improving the performance of the new federal institute. Although the BfArM had been established exclusively for the regulation of pharmaceuticals and medicinal products, it proved to be incapable of achieving sufficient results. This was mainly because of the fact that the BfArM invested heavily in doing preliminary work for European authorization procedures at the expense of applications for the domestic market. With 26 months the average duration of procedures for national marketing authorizations was more than three times longer than required by law. But even though the BfArM had focused very much on its involvement in European regulatory processes it still seemed to be ill prepared to obtain an appropriate position at the European level. According to an official evaluation of the agency's work done by the German Science and Humanities Council ("Wissenschaftsrat") in 2004, the BfArM



clearly underperformed in terms of the frequency of its employment as a “rapporteur” in market authorization applications under the centralized European procedure. Moreover, the Council especially criticized the low engagement in in-house research and an insufficient availability of human resources (Wissenschaftsrat 2004).

These results were considered alarming especially in view of the intention of the EMEA to reduce significantly the number of national regulatory authorities that will participate in future regulatory processes at the European level. As mentioned before, currently there are 47 national agencies that provide scientific expertise and regulatory assistance to the EMEA. In the meantime, however, the European Commission has announced its intention to significantly reduce the number of supporting national agencies by recognizing only a few national “centers of excellence”. It is conceivable that the selection of those centers will most likely depend on their previous performance at the European level. In this respect, a center of excellence in the European pharmaceutical research will be required to act as a full-service agency that is capable of dealing with all areas of medical indication. Apart from that it should also be specialized in a certain field of competence.

Therefore the third step was initiated by the federal government’s reaction to both the results of the evaluation as well as to the plans of the European Commission to reduce the number of national authorities in the European regulatory framework.

In February 2007, it introduced a federal law establishing a new German Agency for Pharmaceutical and Medicinal Products (DAMA). In the official explanatory statement to the law the federal government made explicitly clear that a new institutional structure is needed in order to be able to compete with other member states’ regulatory authorities. The legislative proposal designs the DAMA as a fully autonomous regulatory agency under public law, which will be free to define its organizational routines and to determine the deployment of its financial means and human resources. The DAMA will also follow the example of the EMEA and other European regulatory agencies in view of the role of applications fees of the pharmaceutical industry. In this respect, the federal government

expects that the DAMA's revenues will cover the costs for market authorizations. And finally, the legislative proposal anticipates that the national and international reputation of the DAMA will largely depend on its internal research capacities. It is therefore determined that the DAMA will be obliged to continuously increase its expenditures for research (Deutscher Bundestag 2007).

However, it is remarkable that Germany has not been able yet to accomplish this third step of institutional adaption at the national level. A first attempt to put the related bill through failed in 2005 because of the early elections. Since that election the country is currently by a great coalition with a large majority in the federal parliament. Nevertheless the legislative proposal failed again, because it was shipwrecked by a relatively small number of coalition deputies even before the ballot vote who were worried that the financial contributions from the pharmaceutical industry could undermine the independency of the DAMA. Therefore, as for now the institutional adaption will be going on as a process of reorganization of the BfArM.

### **Conclusions: Germany's Role in Global Pharmaceutical Regulation**

The first aim of this paper has been to discuss the value of the concept of an extended multi-level governance approach for the analysis of those new arrangements of global governance in which the European Union acts on behalf of its member states. One example of such an arrangement is the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, which has made substantial progress towards the harmonization of various regulations regarding pharmaceutical development processes during the last 18 years.

In this respect it has been shown that it was rational for the EU member states to agree on the Europeanization of interest mediation in pharmaceutical regulation. This is mainly because of three reasons. Firstly, a common European engagement within the ICH contributes to the substantiation of the new intra-EU approach towards regulating a single European market for pharmaceutical products. Secondly, the offer to provide a harmonized access to 27 national pharmaceutical markets gives the European

Commission substantial negotiation power that can be used to export European standards to the main important third country markets. And thirdly, the delegation of representation to the European Commission is considered an important contribution to facilitate coherence between the different EU external policies, which affect various aspects of pharmaceutical regulation.

In terms of the extended multi-level governance system (eMLG) it has been further shown that such a system has at least three specific institutional characteristics. Firstly, in an eMLG system regulatory competences are not simply centralized. On the contrary, it is primarily characterized by its non-hierarchical institutional design and by the dynamic dispersion of authority. Secondly, such a system provides for a modus to transform globally agreed soft-law into compulsory Community hard-law and thus guarantees compliance with non-binding international norms. Thirdly, within an extended multi-level governance system the member states come under certain pressure to adapt their domestic institutions. There are reasons to assume that multi-level dynamics may differ to some extent across policy areas. However, the key argument here is that the member states' actual influence on policy processes within such an eMLG system is not primarily determined by their size or relative market power, but by their ability to make use of the multi-level structure. Hence, from a theoretical perspective the most striking aspect of policy-making processes in an eMLG system is that it provides for coordination both by negotiation and competition between member states. Consequently, in order to grasp the complexity of the institutional dynamics within an extended multi-level governance system it is necessary to analyze not only the member states' activities at the European level, but also their domestic adjustments.

Therefore, the empirical aim of the paper has been to look at the German role within the processes of European and Global pharmaceutical regulation. From such a member state's perspective, Germany certainly constitutes a special case. Once a country that dominated the World pharmaceutical market its role has significantly decreased since the second half of the twentieth century. Therefore, the Europeanization of interest mediation should have been a promising strategy to pursue national interests. It has been shown,

however, that such a strategy can also be successful under the condition that national actors succeed in making use of the various channels of interaction within the multi-level system. That is why both national and subnational actors introduced substantial institutional reforms that were aimed at improving their influence at the European level. Moreover, the example of the proposal to establish a new regulatory agency shows that the process of institutional adjustment is far from over. On the contrary, until now Germany did not succeed in adapting to a new “superior” model of pharmaceutical regulation that is characterized by “service-oriented” and “research-driven” regulatory authorities that provide support both to the pharmaceutical industry and the European regulatory network while generating a certain amount of exclusive influence through the development of particular competence areas. In this respect, the DAMA proposal was certainly targeted at this new role model, but – for the time being – failed because of increasing criticism on the appropriateness of close interrelations between regulators and industry.

## References

- Abbott, Kenneth W./Snidal, Duncan, 2000: Hard and Soft Law in International Governance, *International Organization* 54, 421-456.
- Billiet, Stijn, 2006: From GATT to the WTO: The internal struggle for external competences, *Journal of Common Market Studies* 44, 899-919.
- Daemrlich, Arthur D., 2004: *Pharmacopolitics. Drug Regulation in the United States and Germany*, Chapel Hill/London: The University of North Carolina Press.
- Deutscher Bundestag, 2007: Gesetzentwurf der Bundesregierung "Entwurf eines Gesetzes zur Errichtung einer Deutschen Arzneimittel- und Medizinprodukteagentur (DAMA-Errichtungsgesetz), Drs. 16/4374, 23.02.2007.
- Garattini, Silvio/Bertele, Vittorio, 2004: The role of the EMEA in regulating pharmaceutical products. In: Mossialos, Elias/Mrazek, Monique/Walley, Tom (eds.): *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, Maidenhead: Open University Press, 80-96.
- Grande, Edgar, 2000: Multi-Level Governance: Institutionelle Besonderheiten und Funktionsbedingungen des europäischen Mehrebenensystems. In: Grande, Edgar/Jachtenfuchs, Markus (eds.): *Wie problemlösungsfähig ist die EU? Regieren im europäischen Mehrebenensystem*, Baden-Baden: Nomos, 11-30.
- Grande, Edgar, 2001: Institutions and Interests: Interest Groups in the European System of Multi-Level Governance. *Working Paper No. 1/2001, Chair for Political Science*, TU Munich.
- Grande, Edgar/Kaiser, Robert, 2006: The Transformation of the German System of Innovation: The Case of Biotechnology. In: Carayannis, Elias/Campbell, David (eds.): *Knowledge Creation, Diffusion and Use in Innovation Networks and Clusters: A Comparative Systems Approach Across the United States and Europe*, New York: Praeger Publishers (2006), 183-202.
- Gstöhl, Sieglinde/Kaiser, Robert, 2004: Mechanisms of Global Trade Governance: The "Double Standard" on Standards in the WTO. In: Schirm, Stefan A. (ed.): *New Rules for Global Markets: Public and Private Governance in the World Economy*, Basingstoke/New York: Palgrave, 195-213.
- Hooghe, Liesbet/Marks, Gary, 2001: *Multi-Level Governance and European Integration*, Lanham: Rowman & Littlefield.
- House of Commons, 2005: *The Influence of the Pharmaceutical Industry*. Fourth Report of Session 2004-2005, London: House of Commons, Health Committee, March 22, 2005.
- Kaiser, Robert, 2008a: Innovationspolitik. Staatliche Steuerungskapazitäten beim Aufbau wissensbasierter Industrien im internationalen Vergleich, Baden-Baden: Nomos-Verlag.
- Kaiser, Robert, 2008b: Hightech-Policies: Institutionelle Determinanten staatlicher Innovationspolitik im internationalen Vergleich, *Zeitschrift für Politikwissenschaft* 18 (1), 5-24.
- Kaiser, Robert/Prange, Heiko, 2002: A New Concept of Deepening European Integration? – The European Research Area and the Emerging Role of Policy

- Coordination in a Multi-level Governance System, *European Integration online Papers* 6 (2002), No. 18.
- Knodt, Michèle, 2004: International Embeddedness of European multi-level governance, *Journal of European Public Policy* 11, 701-719.
- Kohler-Koch, Beate, 1999: The Evolution and Transformation of European Governance. In: Kohler-Koch, Beate and Eising, Rainer (eds.): *The Transformation of Governance in the European Union*, London/New York: Routledge, 14-35.
- Majone, Giandomenico, 1996: *Regulating Europe*, London: Routledge.
- Permanand, Govin/Altenstetter, Christa, 2004: The politics of pharmaceuticals in the European Union. In: Mossialos, Elias/Mrazek, Monique/Walley, Tom (eds.): *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, Maidenhead: Open University Press, 38-54.
- Peters, Guy B./Pierre, Jon, 2002: Multi-Level Governance: A View from the Garbage Can. *Manchester Papers in Politics: EPRU Series*, 1/2002.
- Scharpf, Fritz W., 1996: Negative and Positive Integration in the Political Economy of European Welfare States. In: Marks, Gary/Fritz W. Scharpf/Philippe C. Schmitter/Wolfgang Streeck, 1996: *Governance in the European Union*. London/Thousand Oaks/New Delhi: Sage, 15-39.
- Schirm, Stefan A., 2004: *Internationale Politische Ökonomie. Eine Einführung*, Baden-Baden: Nomos-Verlag.
- Shelton, Dinah (ed.), 2000: Commitment and Compliance. The Role of Non-Binding Norms in the International Legal System, Oxford: Oxford University Press.
- Vogel, David, 1998: The Globalization of Pharmaceutical Regulation, *Governance* 11, 1-22.
- Wissenschaftsrat, 2004: Stellungnahme zum Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Bonn, Drs. 6102/04, Merseburg 28.05.2004.