

GOVERNING LIPITOR AND LISTERINE: THE DOMESTIC ROOTS OF
INTERNATIONAL PHARMACEUTICAL AND COSMETICS REGULATION

IE Business School Working Paper WP08-17

11-03-2008

David Bach

Abraham L. Newman

IE Business School
Madrid, Spain
david.bach@ie.edu

Georgetown University
Washington, DC
aln24@georgetown.edu

Technical standards and product regulations increasingly shape international trade patterns, the organization of cross-national production, and global investment flows.¹ This paper examines the evolution of international market regulation in the pharmaceutical- and cosmetics industries over the past three decades. International market regulation of pharmaceuticals and cosmetics poses an intriguing empirical puzzle. Both industries have seen the emergence and subsequent institutionalization of international market regulation over the last three decades. In similar ways, the mode of international governance has shifted over time in both cases – from occasional international spill-over of domestic rules to deliberate extraterritorial imposition of domestic laws to transgovernmental cooperation aimed at international harmonization. Yet against this background of commonality, we find a sharp divergence in the sectors when it comes to who exerts most influence: in the case of pharmaceuticals, the United States has long been dominant and has only recently seen its leadership challenged by the European Union; in cosmetics, by contrast, the EU has shaped international market regulation from the outset and the US has failed, repeatedly, to make significant inroads. What explains the similar institutional evolution of international market regulation in the two fields and the sharp divergence in terms of policy influence between them?

INTRODUCTION

Technical standards and product regulations increasingly shape international trade patterns, the organization of cross-national production, and global investment flows.¹ This paper examines the evolution of international market regulation in the pharmaceutical- and cosmetics industries over the past three decades. International market regulation of pharmaceuticals and cosmetics poses an intriguing empirical puzzle. Both industries have seen the emergence and subsequent institutionalization of international market regulation over the last three decades. In similar ways, the mode of international governance has shifted over time in both cases – from occasional international spill-over of domestic rules to deliberate extraterritorial imposition of domestic laws to transgovernmental cooperation aimed at international harmonization.

Yet against this background of commonality, we find a sharp divergence in the sectors when it comes to who exerts most influence: in the case of pharmaceuticals, the United States has long been dominant and has only recently seen its leadership challenged by the European Union; in cosmetics, by contrast, the EU has shaped international market regulation from the outset and the US has failed, repeatedly, to make significant inroads. What explains the similar institutional evolution of international market regulation in the two fields and the sharp divergence in terms of policy influence between them?

We argue that a key to understanding international patterns of interaction – the mode of governance and locus of influence – lies in the sequential development of domestic regulatory capacity in leading markets. Regulatory capacity is the ability of a jurisdiction to define and implement a set of market rules, and to monitor firms' compliance with them. The extent of a jurisdiction's regulatory capacity is largely institutionally-determined. It depends on the number and expertise of staff, the extent of statutory sanctioning authority vested in regulators, and the degree of centralization of regulatory authority over a market.² Jurisdictions with such regulatory capacity are best positioned to project regulatory authority, even beyond their borders if necessary, and can thereby shape international market rules.

Regulatory capacity varies across countries, sectors, and time relative to one another. Disparities in regulatory capacity among leading markets in a given moment in time are therefore quite possible. Like other institutional characteristics of a political economy – such as the financial system, corporate governance, or industrial organization – it is the product of political processes slowly unfolding over time, occasionally even stretching back as far as the era of state- and nation-building.³ Policymakers confronted with new regulatory challenges in the face of globalizing markets must rely on the institutional resources at their disposal, and these usually predate the particular challenge at hand. Jurisdictions can consciously decide to build-up domestic regulatory capacity. For instance, industry liberalization, such as in the case of financial markets or telecommunication, has been associated with a conscious and marked increase in regulatory capacity in many countries.⁴ But such build-up does not happen over-night.

¹ See Raustiala 1997, Vogel and Kagan 2004 and Mattli and Büthe 2003.

² This argument draws on historical institutional work such as Zysman 1994 and Thelen 2004. It builds on work from the domestic setting on bureaucratic autonomy, such as Carpenter 2001 and Goodman 1991. For a recent elaboration in the international setting see Bach and Newman 2007.

³ For the importance of time in causal processes see Pierson 2004 and Büthe 2002.

⁴ See Vogel 1996 and Gilardi 2002.

The relative sequential development of domestic regulatory capacity thus critically shapes patterns of interaction in international market regulation.⁵

Employing the relative sequencing argument, we construct a deductive causal typology, which offers testable expectations about the likelihood of transgovernmental cooperation, extraterritorial application of domestic law, or market governance. Robust transgovernmental cooperation requires capable and domestically-empowered regulators in all the pivotal markets. A highly asymmetric distribution of regulatory capacity across major markets means international market regulation has to proceed through alternative governance modes. Extraterritorial application of domestic rules by the regulatory hegemon is a common form of international market regulation in such instances.⁶ In this case, rather than just controlling market access via product standards, the hegemon imposes its domestic production process proscriptions on foreign producers seeking market access. Lastly, if no jurisdiction has highly-developed regulatory capacity in a sector or those with regulatory capacity choose not to exercise it, pure market coordination prevails internationally. This is the case for new markets at the technological frontier, for instance, where domestic regulation is often entirely lacking.⁷

The paper makes contributions to two critical debates in International Relations. First, it pushes the discussion about the relationship between domestic institutions and international cooperation beyond formal negotiations that take place in the context of traditional liberal intergovernmental bargains.⁸ Most existing work has focused on the role that domestic institutions play when national legislatures are required to ratify international deals.⁹ In an increasing number of instances, this is not the case, as regulators and other substate actors directly engage in international affairs. Secondly, the paper expands on a growing literature concerned with transgovernmental relations. While researchers have demonstrated the ability of such actors to resolve a number of complex global governance challenges¹⁰, there is limited work that predicts the likelihood of transgovernmental cooperation. Transposing historical institutionalist tools, particularly the importance of sequencing and the development of institutional capacity, to the international context we think can push forward these debates.

This paper is organized as follows. The first section gives a brief overview of international market regulation in pharmaceuticals and cosmetics. It describes the surprisingly similar institutional evolution in both sectors and highlights critical difference in terms of the locus of influence between them. Section two examines existing systemic theories of International Relations, emphasizing market size and market friction. Section three sketches a domestic institutional argument that relates changing patterns of interaction in international market regulation to the sequential development of domestic regulatory capacity in leading markets, principally the US and Europe. In the paper's empirical core, we evaluate the expectations of the three approaches through process-tracing. Whereas expectations of existing theories are not or only partially reflected by the evidence, we find that the historical sequence of

⁵ See Newman 2008.

⁶ See, for example, Fox 1997.

⁷ See Spar 2001.

⁸ See Frieden and Martin 2002.

⁹ See Putnam 1988 and Milner 1997.

¹⁰ See Raustiala 2002, Slaughter 2004, Slaughter 1997.

domestic institutional change has indeed shaped patterns of interaction of international market regulation in the expected way. The final section discusses the relevance of the findings for the field of international political economy and draws conclusions for the research program put forth in this special issue.

INTERNATIONAL MARKET REGULATION OF PHARMACEUTICALS

Before entering into the casual debate concerning drivers of international market regulation, we begin with an overview highlighting changing patterns of international interaction. While both sectors experience a layering of extraterritorial efforts and transgovernmental cooperation, the pharmaceutical sector begins with US dominance.

Drug safety and -efficacy have been the motivating drivers of domestic pharmaceutical regulation around the world. The onset of formal domestic pharmaceutical regulation can be dated to the 1906 Pure Food and Drug Act in the United States. During the 19th century, the manufacture and marketing of medicines and health products had been largely a local, artisan affair that was entirely unregulated. Patients took medicines at their own risk. Scientific breakthroughs in medicine, the industrial chemicals revolution, and the prospect of mass production and -distribution considerably increased the stakes. The 1906 Act gave the government a broad mandate to protect consumers by assessing drug safety. In 1938, during the height of the New Deal, Congress delegated authority over the industry to the Food and Drug Administration, an independent regulatory agency. To carry out this mandate, the FDA has asserted authority up and down the value chain, from regulating clinical trials and pharmaceutical manufacturing to supervising drug marketing and advertising. Furthermore, the broad mandate has led the FDA to extend its reach overseas: not only must foreign producers meet all domestic market access requirements, the FDA also conducts inspections of overseas manufacturing facilities if these produce for US consumers.¹¹

The motivating drivers of international market regulation build on existing domestic foundations. As markets have become more integrated, concern has shifted to ensuring safety across jurisdictions – increasingly drugs are developed in one jurisdiction, produced in another, and marketed in a third. To this has been added a dual concern with regulatory efficiency. On the one hand side, pharmaceutical companies demand international regulatory harmonization to reduce transactions costs. The industry has become global yet regulation still requires independent national drug approval, often according to different rules and with incompatible procedures. Secondly, industry globalization has fostered competition between jurisdictions when it comes to the quality, speed, and cost of approval processes.¹²

The mode of governance in international pharmaceutical markets has shifted markedly over time. Initially, international governance consisted largely of the extraterritorial application of US law. Over time governance has moved toward transgovernmental cooperation. Nevertheless, domestic rules promulgated by leading regulators in the US, Europe, and also Japan continue to constitute key elements of international market regulation. Importantly, traditional international organizations have not played a

¹¹ See Vogel 1998 and Lee and Herzstein 1986.

¹² See Wiktorowicz 2003.

prominent role, apart from some OECD-sponsored conferences touting the benefits of harmonization.¹³

Starting in the 1990s, regulators including the FDA have forged bilateral partnerships codified in Memorandums of Understanding (MoU) to promote technical information sharing and coordination. In parallel, regulators from the US, Europe, and Japan launched the International Conference on Harmonization (ICH) to standardize testing and laboratory practices across the world's largest markets. According to one observer, "The accomplishments of the ICH have been impressive. Nearly sixty ICH Topics have become official Guidelines and reached the implementation stage as of 2003, meaning a harmonized text has been approved by all parties, including all three regulatory agencies. Many of these Guidelines pertain to uncontroversial matters in which much international agreement already existed. However, some represent meaningful progress in achieving harmonization."¹⁴ Examples of the latter category include common definitions of such issues as toxicity tests and clean laboratories. However, these efforts did not include a process for joint market approval. Separately, EU and US policymakers have sought to go further, concluding a Mutual Recognition Agreement (MRA) in 1997 that would have regulators certify some of their counterparts' evaluation procedures and thus lead to limited mutual recognition. Even though FDA resistance has largely stalled mutual recognition, transgovernmental cooperation among the world's leading regulators has become a fixture of international pharmaceutical markets regulation.

The locus of influence in international market regulation of pharmaceuticals has changed considerably over the past three decades. Until the 1990s, the US was the sector's undisputed regulatory hegemon. From very early on, the US had relied on a powerful, independent regulatory agency that governed pharmaceuticals primarily by controlling market access. Throughout the post-war period and into the 1990s, the FDA was the undisputed international regulatory reference point and source of best practices. "The FDA has long provided the public health gold standard for the world," said FDA Commissioner Jane E. Henney in 2001.¹⁵ Because the agency was unrelenting in its insistence that any drug – no matter who produced it or where – that was to be marketed in the US had to go through the same grueling approval protocol as domestically-produced drugs, many foreign producers experienced the FDA's professionalism and meticulousness first-hand. Most feared the mighty FDA a great deal more than their own domestic regulators.¹⁶

Since the 1990s, however, there has been a clear shift toward a much more balanced situation. While the FDA continues to exert considerable influence over the international regulatory agenda, the European Commission, and to a lesser extent the Japanese Ministry of Health, Labor, and Welfare, have become powerful voices. The big three dominate standard-setting and enforcement. It is the national regulators of these three markets that control market access, organize and control transgovernmental cooperation, and set the pharmaceuticals-related agenda of international organizations.

¹³ The only notable exception is intellectual property law, where the WTO – through the TRIPS Agreement – has imposed patent protection for pharmaceuticals rooted in US and European law on its more than 130 members.

¹⁴ Lee 2005, 179-80.

¹⁵ *Biomedical Market Newsletter*, 31 January, 11.

¹⁶ Pilot 2000.

While the FDA has adopted some of the practices of its European counterparts, incorporating user fees and recognizing some foreign trials, it has resisted more comprehensive convergence. At the same time, the European Commission has become an equal player in standard setting debates in the ICH.¹⁷

INTERNATIONAL MARKET REGULATION OF COSMETICS

The motivation and public policy justification for cosmetics regulation closely resembles core elements of the pharmaceuticals regime. The principal focus is also product safety and the protection of consumers. As cosmetics generally do not have medical applications, their effectiveness is less of a public policy concern. Just as in the case of pharmaceuticals, however, globalization and market integration have generated business pressure on governments to reduce transactions costs through regulatory harmonization.

The institutional evolution of international cosmetics regulation mirrors the parallel case of pharmaceuticals. Domestic regulation, often with extraterritorial reach, constitutes a first important pillar of governance. The EU in particular has enacted binding regulation for the sector that strictly regulates which ingredients are acceptable, restricted, or outright prohibited through positive and negative ingredient lists. In the US, in contrast, cosmetics (with the exception of colorants) that are not classified as over-the-counter (OTC) drugs fall under a self-regulatory scheme set up and run by industry.

Mirroring pharmaceuticals, transgovernmental cooperation between domestic regulatory agencies has emerged alongside unilateralism. Regulators from four leading markets – the US, Japan, Canada, and the EU – engage in information sharing under the Cosmetics Harmonization and International Cooperation (CHIC) framework. Meetings have taken place three times since 1999. The group initially focused on the exchange of information about their respective regulatory approaches, safety concerns, and alternative testing methods. Initiatives currently under discussion include the establishment of an international rapid alert system to enhance consumer protection. This process produced minimal results and was considered defunct until the recent reinvigoration in 2007 with the start of the International Cooperation on Cosmetics Regulation between the major market regulators. At the same time, the European Commission and the FDA have agreed to a bilateral exchange of letters whereby the two agencies pledge to share information concerning draft legislation, market defects, scientific opinions, and inspection reports. When compared to transgovernmental cooperation in pharmaceuticals and especially to banking or securities regulation, regulator cooperation in the cosmetics field is rather limited. Interestingly, more established international organizations such as the WTO and WHO have been sidestepped in favor of transgovernmental efforts. And these transgovernmental efforts include only four countries, excluding the major emerging markets in Asia and Latin America.¹⁸

Despite similarities in the mode of governance, in terms of the locus of influence the two sectors sharply diverge. In cosmetics, Europe is the undisputed international regulatory hegemon. Mercosur countries including Argentina, Brazil, Paraguay, and

¹⁷ See Kidd 1996-1997 and Kulynych 1999.

¹⁸ See Blaschke 2005.

Uruguay have all adopted legislation in the late 1990s that includes the European definition of cosmetics and that empowers regulatory agencies to oversee positive and negative lists. The ten members of ASEAN adopted legislation in 2003 that essentially copies European rules. ASEAN countries directly imported Annex II of the European directive, which includes the positive and negative ingredient lists maintained by the EU, into binding local regulation. Japan reformed its legislation in 2001 and moved towards the European model. Similarly, the state of California enacted tough legislation in 2006 inspired by European rules. Lastly, in 2007, China formally banned many substances on the European negative list.

In contrast to some of the other major non-EU markets, the US has so far resisted European convergence pressure. This does not mean that EU regulations have not affected US cosmetics firms or cosmetics firms operating in the US. Compliance with EU regulations is a prerequisite for entering the lucrative EU markets as well as a growing number of markets in Latin America and Asia. Many US firms have found it cheaper to adopt EU standards throughout their global operations rather than producing products with different compositions for different markets. Moreover, in a few cases where cosmetics firms refused to remove ingredients in products for the US market even though these had been banned in Europe, US consumer organizations mobilized and eventually forced product changes for the US market as well.¹⁹ The EU has thus extended its de-facto regulatory reach around the world, including to the US

The Empirical Puzzle

The evolution of international market regulation in both pharmaceuticals and cosmetics poses a puzzle for IPE scholars. The patterns of interaction in the two sectors have changed considerably over the past three decades, both in terms of mode of governance and in terms of locus of influence. In both cases we see a gradual evolution of international market regulation, driven initially by the extraterritorial application of domestic rules, i.e. the deliberate exercise of authority outside of a jurisdiction's physical borders. The FDA took the lead in pharmaceuticals and ensured that foreign producers met strict US safety norms and standards, not just for the products themselves but also regarding drug development and production. Conversely, in the cosmetics case, Europe has asserted influence and has extended the de-facto reach of European regulation far beyond the continent. In both cases, unidirectional regulatory exports are being complemented with transgovernmental regulatory cooperation, i.e. direct interaction among sub-state units in semi-autonomous fashion from their national executive.

How can we explain the changing patterns of interaction in both sectors? What explains the remarkably similar evolution of international market regulation from extraterritorial application of national law to transgovernmental cooperation? And why do the two cases diverge so sharply when it comes to who has exerted most influence over policy? In the pharmaceutical case, a long period of US regulatory hegemony is slowly giving way to a more balanced situation as the EU has begun to assert influence. In cosmetics, in contrast, Europe has been and remains the undisputed regulatory hegemon. What explains this sharp empirical divergence in two closely-related industries?

¹⁹ See Laurel Naversen Geraghty, "Should You Worry About the Chemicals in Your Makeup?," *The New York Times*, July 7, 2005.

EXPECTATIONS OF EXISTING THEORIES: MARKET SIZE OR MARKET FRICTION

Before presenting our model of comparative institutional sequencing, we derive relevant expectations from the two dominant theories used to explain patterns of international economic governance. After the presentation of the theoretical expectations of existing approaches and our own argument, we use the historical narratives as a process tracing exercise to test the usefulness of the competing causal mechanisms. As the outcome of interest – patterns of interaction – is not disputed, the focus of the paper concerns the alternative causal claims that might have produced the outcome.

Market Size

Realist theories of international cooperation and international political economy focus attention on the decisive role of state power.²⁰ Recently, scholars have applied realist thinking to the field of international market regulation.²¹ Power here is taken to be market power, which is usually operationalized through a focus on market size. As Drezner explains, “[s]tates are differentiated by their relative power” and “[p]ower is defined as the relative size and diversity of an actor’s internal market.” According to realists, dominant powers – those with the largest markets relative to others – should be able to decisively shape international market rules, either through extraterritorial reach or within international bodies. Shifts in the locus of influence should reflect changes in relative market size.²² As such, the US, EU, and Japan, which have the largest markets in both sectors, should be the pivotal players. But beyond the expectation that the major markets should drive international market policy, the theory is indeterminate. Assuming a more or less equitable distribution of market power among the major markets, the most likely result from a realist perspective would be rival regulations promoted by the respective camps.

In terms of the mode of governance, realist theory does not make a clear prediction. Recent work by Drezner suggests that a hegemon may look to non-traditional actors to obtain outcomes that they themselves find costly to achieve. Ultimately, transgovernmental networks are expected to serve the dominant powers’ national interests. But that merely raises the question why dominant powers would prefer one mode of governance to another. There is no clear expectation that explains a shift from extraterritorial application of national laws to transgovernmental cooperation. Realist theory, then, offers clearer expectations concerning the locus of influence as opposed to modes of governance.

Market Friction

Functionalist theories of international cooperation in a liberal tradition stress the underlying collective action problems, externalities, and inefficiencies that generate demand for international regimes.²³ States, in turn, supply regimes to reduce transaction costs associated with international interdependence. The states that experience the most inefficiencies from the system are, then, most likely to press for and shape cooperation.

The mode of governance will reflect the underlying collective action problem with greater centralization and delegation as transaction costs increase. Among the most

²⁰ See Krasner 1976, Krasner 1991.

²¹ See Drezner 2007.

²² See Aggarwal 1985, James and Lake 1989, Shambaugh 1996.

²³ See Keohane 1984, Keohane 1983, Martin and Simmons 1998.

important functions performed by international regimes are the provision of information and the facilitation of credible commitments by participating states.²⁴ The effective provision of information often requires the creation of a centralized coordination body, such as the Organization for Economic Cooperation and Development (OECD). But if information provision alone is the goal, no formal independence from participating states is necessary. However, if the institution is also to help states make credible commitments, it must have a measure of independence from its members, such as, for example, the World Trade Organization (WTO). Networks, by contrast, tend to be informal, voluntary, and decentralized.

The theory expects that given high levels of international interdependence states would seek institutional means to share information, promote reciprocal learning, and foster consensus driven harmonization. In the case of international market regulation, where firms confront disparate national regulations across markets, states with large and diverse export markets suffer the greatest burden. States should have little incentive to invest in international cooperation where national firms focus primarily on the domestic market and the country is primarily an import market. They have the luxury to free ride on the efforts of those suffering the greatest transaction costs.

The institutional form chosen performs the required functions at the lowest cost. Network-based transgovernmental cooperation, for example, would be most likely when there is demand for information provision and coordination but no need for a strong hierarchy that could make a mutual commitment credible.²⁵ A lack of cooperation, in turn, would suggest that any benefits of reduced transaction costs are outweighed by other costs. If, in such cases, transactions costs are sufficiently high to render pure market coordination inefficient, states might try to apply domestic rules extraterritorially.

Figure 1: Expectations of Existing Theories

| | Realism | Liberalism |
|---------------------------|---|--|
| Mode of Governance | determined by preferences of dominant power(s) | determined by nature of collective action problem, externalities, and inefficiencies |
| Locus of Influence | determined by distribution of power, which is reflected in relative market size | determined by relative transaction costs, which is shaped by extent of interdependence |

REGULATORY CAPACITY, SEQUENCING, AND INTERNATIONAL MARKET REGULATION

Building on historical institutionalist tools, we derive an alternative causal logic to explain evolving patterns of interaction based on the relative sequential development of domestic regulatory capacity in leading markets. Regulatory capacity is a jurisdiction's ability to define, monitor, and enforce a set of domestic market rules. It encompasses

²⁴ See Abbott and Snidal 1988.

²⁵ See Kahler forthcoming, Kahler and Lake 2003.

the institutions that implement regulations, the expertise of staff working for these institutions, and the overarching coordination of such institutions within the political economy. Clearly, regulatory capacity can vary across sectors and policy areas. A jurisdiction's regulatory institutions may be well-developed in the field of banking regulation, for example, but weak in competition policy or utilities regulation. And like all institutions in a political economy, regulatory institutions develop over time and relative to other political and institutional developments, at home and abroad. Let us first elaborate the concept of regulatory capacity and explain how it bears on international market regulation, and then turn to sequencing.

Regulatory Capacity

International market regulation is rooted in domestic institutions. Jurisdictions build regulatory regimes for domestic markets over time. In doing so they draw on available institutional resources and patterns.²⁶ Fundamental characteristics of political economy, such as the nature of state-society relations or the administrative capacity of the state that are rooted in historical trajectories of state- and nation-building, come to shape the institutional configuration of domestic market regulation.²⁷ This does not mean that regulatory capacity does not change. The American progressive era, for example, saw a considerable expansion of regulatory capacity, especially on the federal level.²⁸ Similarly, the rise of the regulatory state around the world has considerably augmented regulatory capacity in many sectors.²⁹ But such changes are generally quite slow.³⁰ When regulators confront new challenges at $T=1$, they must usually do so with institutional resources developed at $T=0$. With respect to international market regulation this means that regulators initially confronted the challenges posed by globalization and market integration with regulatory tools developed for domestic settings. Only over time have domestic institutional reforms altered the tools for international market regulation.

Regulatory capacity is a multidimensional construct interlinked through a set of institutional complementarities.³¹ A jurisdiction's regulatory capacity in a given industry and point in time depends on its regulatory expertise, the coherence of regulation, and the extent of the regulator's sanctioning authority. To be effective, regulators need the staff and technical expertise to identify new challenges and to formulate and implement countervailing regulatory strategies. Regulatory authority also has to be coherent. Institutional fragmentation and/or poor coordination among regulatory sub-units undermines a jurisdiction's regulatory capacity. Lastly, regulatory capacity depends on the extent of a regulator's statutory sanctioning authority. Sanctioning tools range from public shaming through fines all the way to formal market exclusion. All else equal, regulators that are institutionally empowered to exclude from the domestic market have greater regulatory capacity than those that are not.

²⁶ See Evans, Rueschemeyer, and Skocpol 1985.

²⁷ See Hall 1986, Zysman 1983.

²⁸ See Skowronek 1982.

²⁹ See Moran 2002.

³⁰ See Thelen 2004.

³¹ See Bach and Newman 2007, Mattli and Büthe 2003.

International Implications

The importance of regulatory capacity is that it is the missing link between market size and international regulatory influence.³² A sizeable market alone does not confer regulatory influence. To wield international influence, jurisdictions need capable and powerful domestic regulators that can identify new challenges posed by globalization, formulate countervailing strategies, and enforce rules where necessary even against foreign opposition. Jurisdictions with large markets rely on their institutional resources to make demands on foreign jurisdictions. Those foreign jurisdictions, in turn, make domestic adjustments when perceived costs of resisting are greater than the cost of adjustment. Internationally influential domestic regulators must be institutionally empowered to punish foreign failures to adjust. Sanctioning tools range from exacting reputational costs associated with condemnation through official administrative fines all the way to exclusion from the domestic market. The size of the domestic market thus matters a great deal because it determines the extent of *potential* resistance costs. It does not determine the *actual* cost of non-adjustment, however, because the *probability* of sanctioning is not given by market size but rather by the credible threat of discovery and enforcement. The critical variable in the influence equation is thus the foreign jurisdiction's perception of the demand-making regulator's ability to monitor and punish inaction, a political institutional – as opposed to purely economic – variable.³³

In contrast to our predictions, research applying the Schelling Conjecture to international negotiations has argued that internal fragmentation strengthens a jurisdiction's international bargaining position.³⁴ The threat of domestic veto ties the hands of the international negotiator. This work, however, assumes that international negotiators, in the context of liberal intergovernmental agreements, face a domestic ratification requirement. They may then use the ratification requirement to tie their hands and force compromise. In international market regulation, by contrast, formal negotiations with ratification requirements are rare.³⁵ Rather, states proceed through transgovernmental cooperation or react to extra-territorial application of national laws. In both cases, the domestic regulator is simultaneously the international actor, collapsing the 2-level game metaphor. In these cases, it is the ability to provide a coherent first move or send a knowledgeable expert to the table that produces results both of which require significant regulatory capacity.

Domestic regulatory capacity develops over time, but it does so unevenly across jurisdictions. This produces a relative sequencing dynamic that profoundly shapes patterns of interaction in international market regulation.³⁶ Interjurisdictional unevenness, which is not uncommon, can be dubbed the "Kissinger Effect." As US Secretary of State, Henry Kissinger underscored transatlantic asymmetry resulting from insufficient political integration in the Old World: "Who do I call if I want to call Europe?," he asked succinctly. Similar asymmetries also profoundly affect international market regulation. If there is no institutionally-empowered counterpart to negotiate with, regulators in leading markets may have little choice but to apply domestic rules extraterritorially in order to safeguard the domestic status quo in the face of market

³² See Bach and Newman 2007, Newman 2008.

³³ See North and Weingast 1989.

³⁴ See Meunier 2005, Putnam 1988

³⁵ See Knopf 1993 and Büthe 2007.

³⁶ This transposes sequencing arguments developed in the comparative setting to international issues. See Pierson 2000.

globalization. Domestic early adopters thus often have a first-mover advantage when it comes to substantive international market rules, though they may be faced with the difficult task of unilaterally setting and especially enforcing rules.³⁷

The logic of relative sequencing implies that a first-mover advantage may not last forever. Follower jurisdictions may develop their own regulatory capacity. This can occur as an unintended consequence of domestic regulatory reform, or as a deliberate response to the first-mover's international assertion of authority. In either case, the expansion of regulatory capacity in a key follower jurisdiction is a necessary condition for the development of more formal transgovernmental cooperation. International market regulation thus evolves, as transgovernmental cooperation complements or displaces unilateral moves. If both leading markets have insufficient regulatory capacity or are otherwise unwilling to assume an international role, pure market coordination prevails. Figure 1 summarizes the expected effects of the distribution of regulatory capacity on the form of international market regulation.

Figure 1: Domestic Regulatory Capacity and International Market Regulation

| | | A's Regulatory Capacity | |
|-------------------------|------|----------------------------|-------------------------------|
| | | Low | High |
| B's Regulatory Capacity | Low | Market Coordination | Extraterritorial Push A=>B |
| | High | Extraterritorial Push B=>A | Transgovernmental Cooperation |

But why would a regulatory first-mover even consider sharing authority and engaging in cooperation? There are two reasons. First, governing internationalizing markets via extraterritorial application of domestic rules is costly and often inefficient. Costs occur both in terms of monitoring and, more importantly, in terms of business lobbies pushing for greater harmonization and less market friction. Secondly, the follower jurisdiction – now drawing on its own regulatory capacity – can make costly demands on the initial first-mover. It can push its own rules extraterritorially, for instance. Power in international market regulation can thus be usefully thought of as the ability to unilaterally shift the reversion point for international bargaining. The reversion point describes the set of international market rules that prevail in the absence of a new international agreement.³⁸ Domestic regulators that acquire new competencies – competencies that enable them to unilaterally change aspects of the international market environment – wield additional influence in formal or informal international bargaining.

The domestic institutional argument leads to the following expectations about international market regulation. The domestic institutional status quo in leading markets just prior to the onset of international market regulation strongly shapes broad institutional contours of international governance in a sector. If regulatory state-type institutions existed, we should expect domestic regulatory agencies to play leading roles in any evolving international regime. Pronounced asymmetry of domestic regulatory regimes in terms of institutional design and/or regulatory capacity – the “Kissinger Effect” – skews international governance towards unilateral mechanisms and hinders

³⁷ See Newman 2008.

³⁸ See Richards 1999.

sustained international cooperation. Institutional reform in follower states, however, can make the international distribution of regulatory capacity less lopsided and thus enable transgovernmental cooperation.

Relative sequencing also affects who gets to shape the initial international regulatory agenda. A regulatory first-mover with the ability to unilaterally shift the reversion point can obtain critical leverage over the evolving regime. Beyond sequencing, a jurisdiction's ability to promote its rules internationally depends on the extent of its domestic regulatory capacity. The extent of regulatory expertise, coherence, and sanctioning authority determines a jurisdiction's ability to monitor and enforce its rules, thus providing incentives for foreign adjustment. This means that jurisdictions with greater regulatory capacity may be able to shape international market regulation even when there is relative parity in market size. While existing arguments focusing on market size predict opposing camps and rival rules in the case of relative market parity, we argue that discrepancies in regulatory capacity can decidedly tilt the balance toward one camp. This is because regulatory capacity can impose non-adjustment costs even on comparably large markets. Regulatory hegemony may thus result despite preference conflicts among the dominant powers.

In the following section, we trace the competing causal expectations highlighted above through the historical narrative of the two sectors.

TRACING PHARMACEUTICAL REGULATION

From the onset of market globalization in the pharmaceutical industry and well into the 1990s, the US was the dominant regulatory force in international markets. Unwilling to even consider modifications of its strict domestic standards, US regulators frequently imposed their own rules extraterritorially on foreign producers. The situation started to change in the 1990s, with both the mode of governance and the locus of influence shifting. Extraterritorial imposition of US rules gradually gave way to regulatory cooperation among the US, EU, and Japan. And after decades of near-hegemony in international pharmaceutical market regulation, Europe began to openly challenge US leadership. Indeed, powerful US regulators for the first time have had to make meaningful concessions to foreign authorities. How do the three principal explanations – realist, liberal, and domestic institutional – fare?

Market Size

Realists attribute broad contours of international regulatory regimes to the interests of dominant powers. Power, in this context, generally refers to market power for which market size or global market share are frequently used as proxies (Drezner 2006). The main focus of a realist inquiry is the locus of influence, i.e. who controls the policy agenda? Institutional aspects of governance are secondary as these are assumed to be determined by the dominant powers' interests and reflective of the underlying distribution of power.³⁹ Realists thus make straightforward predictions about the variables that should produce the empirical pattern described above: US regulatory hegemony into the 1990s was a reflection of US market dominance. The gradual balancing of influence and onset of greater cooperation, in turn, should be due to an

³⁹ Krasner 1991.

underlying structural change in the market, away from US dominance and toward a more balanced distribution of market power.

Surprisingly, the data for worldwide pharmaceutical sales and production tell a completely different story. In 1990, the European Union accounted for 37.8 percent of the roughly €136 billion global market for pharmaceuticals. The US was in second place with 31.1 percent. In 2003, with the total market almost three times the size at €412 billion, the US now represented a whopping 49.1 percent compared to only 27.8 percent in the post-enlargement EU.⁴⁰ Whereas the industry had grown in the preceding decade at an annual rate of 4.6 percent in Europe, US annual growth was more than double at 9.3 percent.

A similarly perplexing pattern is shown by data on the location of research expenditures, a key indicator as much pharmaceutical regulation focuses precisely on procedures for drug research, development, and testing. In 1990, the pharmaceutical industry spent about €8 billion on research and development in Europe as compared to only €5.3 in the US. A decade later, the picture was completely reversed. By 2001, the industry as a whole invested €26.4 billion in research and development in the US and a mere €18 billion in Europe.

Despite intense market competition and industry consolidation, there has also been no fundamental change in the balance of power between US and European pharmaceutical firms. In 1997, US firms accounted for 50.2 percent of global sales by the ten largest pharmaceutical firms, compared to 28.9 percent for firms incorporated in the EU. These figures had risen to 51.4 percent for US firms and 32.7 percent for EU firms by 2002.

In sum, US market power should have markedly increased over the principal period under investigation. Rather than Europe catching up as far as market size is concerned and thus challenging US market hegemony, as the realist argument would suggest, we see the opposite: a balanced market picture with even a slight European edge in the early 1990s has given way to clear international market dominance by the US. Instead of a close linear correlation of market size and regulatory influence as realist theory would suggest, we find an inverse relationship between the two principal variables.

Market Frictions

To explain international governance, liberal functionalists focus attention on the underlying inefficiencies and transaction costs that generate demand for international cooperation and international institutions.⁴¹ Countries with the highest level of international interdependence in a given industry have the most to gain from international harmonization and are therefore expected to drive international cooperation. Indeed, we find that the ten largest importers of pharmaceuticals are the US, Japan, and eight European countries. These ten markets' overall share of imports has steadily increased, from 50.9 percent in 1980 to 61.8 percent by 1990 and 63.3 percent in 1999. Similarly, the US and nine European countries are the ten largest pharmaceutical exporters, accounting for 76.4 percent of world pharmaceutical exports in 1980, 73.7 percent in 1990, and 79.8 percent in 1999. Much pharmaceutical trade consequently occurs among the handful of leading markets. During this period, overall

⁴⁰ IMS Health 2004.

⁴¹ See, for example, Simmons 2001.

trade in pharmaceuticals has exploded, growing from a mere \$5 billion in 1980 to almost \$120 billion by 1999 in constant prices.⁴²

At first sight, the data are consistent with the basic liberal explanation for international cooperation. A handful of countries account for the lion's share of pharmaceutical trade, both imports and exports, and these countries have been most active in international market regulation. The economic stakes have also markedly increased, both in terms of absolute trade volumes and their importance relative to GDP: the share of pharmaceutical trade for the US, Germany, France, the UK, and Japan, for example, has more than doubled, from 0.2 percent of these five major economies' GDP in 1980 to 0.48 percent by 1999. In light of the growing importance of pharmaceutical trade and the high level of interdependence among markets in the US, Europe, and Japan, it is clear that these markets have the most to gain economically from international regulatory harmonization.

Despite these consistencies, a liberal account of international market regulation in pharmaceuticals centered on transactions costs and economic gains from harmonization leaves key pieces of the empirical puzzle unaddressed. First, arguments stressing market friction and international interdependence cannot explain the shift from extraterritorial application of US law to transgovernmental cooperation. Interdependence has gradually increased, yet the shift in governance in the 1990s is comparatively sudden. Liberals ordinarily attribute significant institutional change in governance to a change in the underlying collective action problem or externality that drives cooperation. But it is not clear what functional change this could be in the case of pharmaceutical. Secondly, the liberal argument does not shed light on the shifting locus of influence in international pharmaceutical regulation. US hegemony has given way to a more balance transatlantic situation in which regulators from Europe and the US learn from one another, share information, and standardize procedures. Thirdly, in light of the rapid growth of global pharmaceuticals markets and the persistent market friction stemming from continued regulatory heterogeneity, it is surprising that regulatory cooperation among major markets has remained fairly limited. The US in particular has shown the least interest in harmonization, even though US firms are among the most global and the domestic US market is among the most internationally integrated.

Regulatory Capacity

A third potential explanation for the empirical picture painted above focuses on the sequential development of regulatory capacity in the major markets. The institutional development of domestic pharmaceutical market regulation has proceeded along very different paths in the US and Europe. Whereas US regulators confronted the period of market globalization with considerable regulatory capacity – manifested by significant expertise, regulatory coherence, and sweeping powers –, their European counterparts acquired similar capacity much later. In-between, transatlantic regulatory asymmetry prevailed, what we call the “Kissinger Effect”.

The construction of powerful regulatory state-type institutions in the US began in the early part of the 20th century. The 1906 Food and Drug Acts gave the government a broad mandate to assess the safety of drugs and in 1938 Congress delegated authority to

⁴² The World Medicines Situation 2004, ch. 3.

carry out that task to the FDA, an independent regulatory agency. The agency quickly and consciously built in-house technical expertise. To carry out its mandate, the FDA got involved in many aspects of pharmaceutical research, -development, and -marketing, including oversight of laboratory conditions, testing methods, human trial protocols, and post-market safety. But its most fundamental task – and the principal source of its power – is its market gatekeeper function. New drugs need FDA approval before they can be marketed, thus granting the agency sweeping market exclusion power. With a single agency in charge counting on expert staff and sweeping market exclusion power, the FDA epitomizes extensive regulatory capacity.⁴³

In contrast to the early, relatively quick development of considerable regulatory capacity in the US, most industrial countries lacked a formal regulatory regime well into the 1960s. Britain and Germany, for example, relied on voluntary safety reporting systems run by the industry. Companies and trade associations played the primary role in regulating product development and market entry, resulting in an informal, decentralized governance structure.

These informal systems came under intense pressure after a series of public health scandals. The thalidomide crisis of the early 1960s, in which a drug given primarily to pregnant women to combat morning sickness produced extreme birth defects, demonstrated the failure of informal drug approval regimes. The drug had been developed by a German company and was marketed in many countries without testing for effects on the health of the fetus. Over 8000 infants were affected globally. In the US, however, the FDA had rejected market approval for the drug citing concern for the safety of fetuses. The fallout from the scandal prompted both the UK and Germany to move toward the US model of formal governmental oversight by professional regulators, though the legislative reforms took decades to be fully implemented. The sharp contrast between the two models' performance helped establish the FDA as the undisputed global reference point for drug approval.⁴⁴

If the thalidomide crisis had demonstrated the US model's superiority, the 1970s and 1980s saw a slow and barely noticeable shift in pharmaceutical regulation on opposite sides of the Atlantic. Congress' response to the thalidomide scare was to further expand the FDA's regulatory authority. Most importantly, it added efficacy to safety as a requirement for FDA drug approval. It also expanded the protections given to participants in clinical trials, including informed consent for human subjects, and established mandatory reporting requirements for drug companies of adverse drug reactions. While further strengthening US regulatory capacity, the unintended consequence of these reforms was a marked increase in the time needed to obtain US market approval. Average drug development times in the US ballooned from 8.1 years in the 1960s to 14.2 years by the 1980s and much of the increase was attributable to the demands of more stringent regulation.⁴⁵ The onset of industry globalization in the 1970s began to turn this into a political issue, as US drug makers increasingly felt cumbersome US regulation put them at a competitive disadvantage in integrating markets.

⁴³ See Kulynych 1999, Wiktorowicz 2003.

⁴⁴ See Lee and Herzstein 1986, Wiktorowicz 2003.

⁴⁵ DiMasi 2001.

At the same time European countries accelerated the development of their own regulatory state-type institutions for pharmaceuticals. The European Community entered the debate in 1965 in the immediate aftermath of the thalidomide crisis and adopted a directive that required the formalization of pharmaceutical market regulation. Implementation was left to member states, however, prompting the development of nationally-distinct regulatory systems. What followed was a 30-years struggle to progressively harmonize and integrate European pharmaceutical regulation. In 1975, the European Commission introduced a procedure enabling drug companies to submit regulatory approval in one member state to authorities in other member states. While the initiative signaled the first step toward transnational pharmaceutical regulation, member states used multiple exemptions in the directive to stall implementation. The transnationalization of regulation took another important step in 1983 when the Commission created a standing committee of national regulators, the Committee for Proprietary Medicinal Products (CPMP), planting the seeds for an eventual pan-European pharmaceuticals regulator. Still, the European market remained fragmented among member state lines. The Commission identified lack of regulatory harmonization as a principal obstacle to greater market integration and pushed for even greater centralization of regulatory authority. A 1993 directive gave authority for the approval of innovative drugs to the CPMP, required national regulators to justify any deviation from a prior decision by another member state regulator, and created the European Agency for the Evaluation of Medical Products (EMEA, later renamed the European Medicines Agency, EMA). The agency centralized regulatory expertise at the EU-level and became the institutional anchor for the CPMP network of national regulators.⁴⁶

By the early 1990s, the regulatory structure of the European pharmaceutical sector had undergone two fundamental transformations. First, informal industry-led governance had been replaced by formal regulatory state-type institutions at the national level. Secondly, the European Commission began to coordinate these consolidated regulatory institutions at the European level and increasingly centralized regulatory authority at the EU level. The result was a marked increase in European regulatory capacity over pharmaceuticals.⁴⁷ The professionalization and cross-national coordination of regulation greatly expanded regulatory expertise. Furthermore, Commission coordination and centralization of authority via CPMP and EMA boosted regulatory coherence, giving Europe a single voice. Finally, the new institutions controlled access to the now-integrating European pharmaceutical market, a powerful source of international leverage.

Sequencing and its International Implications

The sequential development of regulatory capacity on opposite sides of the Atlantic fits with the observed evolution of international market regulation. US international dominance into the 1990s stemmed from unrivalled US regulatory capacity in the industry. During this period, the simplest response to the challenge of dissimilar national regulation amidst market integration was the extraterritorial application of US law. Yet market integration exposed US firms to foreign approval systems, many of which had improved considerably since the 1960s while maintaining quick approval times. A major reason was that industry associations continued to play important roles in Europe and Japan. Moreover, non-US regulators charged evaluation fees to

⁴⁶ See Feick 2002

⁴⁷ See Kidd 1996-1997, Vogal 1998.

outsource aspects of drug evaluation to private contractors. In the US in contrast, the FDA continued to rely exclusively on in-house experts, slowing down the process and making it increasingly bureaucratic. The difference between the systems became a political issue in the 1980s when US drug makers decried a “drug lag” which they claimed challenged their international competitiveness. The result was growing pressure on the FDA to abandon unilateralism and to start looking abroad for new ideas. At the same time, European regulatory capacity had increased considerably as a result of domestic institutional reforms and pan-European coordination and centralization of regulatory authority. The picture captured by the “Kissinger Effect” gave way for a more symmetrical distribution of regulatory capacity. The stage was thus set for an institutional shift in international market regulation, away from pure unilateralism and towards regulatory cooperation.

In a dramatic reorientation, the FDA – over the span of just a few years in the early 1990s – established an Office of International Affairs, signed Memorandums of Understanding with foreign regulators, and lifted restrictions on information sharing with foreign authorities. Together with the European Commission, Japanese authorities, and various industry associations, the FDA launched the International Conference on Harmonization in 1991 to reduce friction in international pharmaceutical markets. The agenda initially focused on information sharing and best practice development. A major milestone was reached when the three parties agreed on a Common Technical Document (CTD). The procedure, hailed as an “enormous achievement,” standardizes the documentation necessary to initiate the approval process in the three regions, though it does not harmonize the actual regulatory processes or requirements.⁴⁸

Efforts to harmonize drug approval further have been less fruitful, especially because of FDA opposition. As part of an effort to lower regulatory barriers to transatlantic trade, policymakers from the US and EU signed a Mutual Recognition Agreement in 1997 that included pharmaceuticals. The MRA does not harmonized regulation. Rather, the idea was to allow European regulators to certify on a case-by-case and ongoing basis that European exporters comply with US quality and safety standards, called Good Manufacturing Practices, and vice versa. This would have eliminated the need for overseas inspections and dual filing of compliance documentation. However, the FDA has largely failed to implement the accord and overseas inspections continue. In return, European regulators acting on behalf of EMEA have expanded their inspections of US manufacturers seeking to export to Europe and, in the words of one executive, EMEA audits “tend to be much harder than FDA” domestic audits.⁴⁹

Despite the failure to secure full mutual recognition, cooperation remains robust. The FDA and European Commission now meet regularly under the 2005 Roadmap for Transatlantic Regulatory Cooperation. As a result, cooperation in some areas, such as scientific consultation in the field of biotechnology, is now firmly institutionalized. And lack of sweeping international deals does not mean there has not been convergence. Enhances direct and indirect exposure to its European counterparts has triggered some important substantive changes in FDA practices. In 1992, for example, the US regulator copied the European model of charging for drug approval and channeling the

⁴⁸ Molzon 2005, 449.

⁴⁹ See “EMEA inspections growing, get tougher than FDA audits, Wyeth exec says,” *Warning Letter Bulletin*, 12 July 2004.

monies into expanded resources and speedier reviews.⁵⁰ Five years later, the FDA took another page out of Europe's regulatory playbook when it authorized the use of third-party assessment of drug safety. In short, while regulatory cooperation in pharmaceuticals remains limited, there has been a remarkable turnaround: what used to be a one-way street has given way to a more balanced situation of mutual learning and cooperation is increasingly displacing simple extraterritorial application of domestic rules. Whereas realist and liberal arguments stressing market size and market friction struggle to account for this development, an assessment of the sequential development of regulatory capacity in key markets offers a compelling explanation.

TRACING COSMETICS REGULATION

International market regulation in the area of cosmetics lagged considerably behind pharmaceuticals. Through the 1970s, most regulatory debates occurred at the national level with growing regional cooperation in Europe. Since the 1980s, Europe has played the dominant position in international markets, defining laboratory best practices and exporting its regulatory model around the world. Since the year 2000, there have been several initiatives to expand transgovernmental cooperation between regulators from the three major markets. Despite these initiatives, the fundamental characteristics of international market regulation have remained unchanged: Europe wield's tremendous regulatory influence and extra-territorial extensions of European law continue to be the principal source of international governance.

Market Size

An economic realist would expect European influence in international cosmetics governance to stem from its relative market size. Convergence on the European model by Latin American and Asian markets could be explained through growth in the European market over the last decade and the associated "gravitational pull" that Drezner and others have highlighted.

Actual market numbers present a mixed picture. Western Europe has the largest single regional market for cosmetics with 29% of the global \$270 billion market in 2006. North America, however, was close behind with 21%. Both regions have seen their share of the world market fall since the late 1990s from 31% and 25% respectively. During this entire time, the United States has had the largest single national market. Japanese world market share has remained relatively constant at 11% since 2003.⁵¹

Turning closer attention to dynamic market changes, evidence does not point to rising European fortunes. Recent sector growth is centered in Latin America and emerging economies in Asia and not in Western Europe or North America (where annual market growth rates were only 3% and 2% between 2001 and 2006). While the United States, Japan, France, Germany, the United Kingdom, and Italy represented the six largest national markets in 2003, Brazil has surpassed France as the third largest and China has moved passed Italy to become the seventh largest market in 2006.⁵²

Europe, then, is the current global market leader in cosmetics but does not enjoy the role of market hegemon as say the United States did in the financial services sector for much

⁵⁰ See FDA Reform and the European Medicines Evaluation Agency 1995.

⁵¹ Data are taken from presentations made in April 2004 and April 2007 by Euromonitor.

⁵² Data are taken from presentations made in April 2004 and April 2007 by Euromonitor

of the 1980s and 1990s. Market size cannot explain the vigor with which Europe has promoted its regulatory model compared to the relative absence of the US in similar global discussions. Interestingly, the market size argument correctly predicts the relatively junior partner status that Japan plays. The shift by China, Japan, and other large markets, however, toward the European regulatory approach in recent years is not clearly explained from shifts in relative market size.

Market Frictions

A second set of arguments focuses on the transaction costs associated with market interdependence. Governments adjust their domestic regulations in order to minimize the frictions that arise from dissimilar rules. One would expect high levels of cooperation between markets characterized by high levels of interdependence.

Once again, market data does not clearly support the expectations of the liberal functionalist claims. The European Union and the United States have long been net exporters of cosmetics and are each other's largest export market.⁵³ In terms of foreign sales and asset dispersion, European and US firms are similarly integrated into world markets. In 2003, over 20% of sales for the largest European and American cosmetics firms happened in each other's markets and a similar percent of assets were located inter-regionally. These firms received roughly 17% of their sales in Japan, bringing foreign sales to roughly 40% of the total. The Japanese sector is much less integrated into the global economy. Japanese companies control some 70% of their home market. In 2003, the largest Japanese firms were much more dependent on their domestic market with only 8% of sales coming from Europe and the United States combined and only 13% of assets located in those other two regions.⁵⁴ Since the late 1990s, Japan was a net importer of cosmetics products and in recent years has found its exports to the European Union and the United States eclipsed by China.

Given these economic patterns of interdependence with the United States and Europe highly integrated and Japan relatively independent it is surprising, at least from a liberal functionalist perspective, that the United States has shown the least interest in global cooperation. The United States, which along with Europe has the most to gain from standardization, is the least active. Similarly, the theory would not predict Japanese engagement in regulatory cooperation or its reform of its domestic regulatory system in line with European rules.

Relative Efforts at Constructing Regulatory Capacity

Transatlantic cosmetics markets exhibit an extensive "Kissinger Effect", though in the opposite direction: whereas US regulatory capacity is fragmented and low, the EU boasts powerful regulatory state institutions and strong coordination at the EU-level. The institutional development of the regulatory state in the two largest cosmetics markets built very distinct regulatory legacies, which continue to shape international market regulation today. In the US, the Food, Drugs and Cosmetics Act of 1938 required that cosmetics be safe but it failed (with the exception of colorants) to provide the FDA with pre-market approval power. Many consumer advocates criticize the lack of FDA oversight, noting that the agency has not defined "safety" for the sector. It was not until 1976 that the Cosmetic, Toiletry & Fragrance Association organized the Cosmetics Ingredient Review as a voluntary, self-regulatory governance mechanism.

⁵³ See Global Insight 2007.

⁵⁴ See Oh and Rugman 2006.

The FDA has in practice no formal authority to control market access and has comparatively little expertise in the issue, relying instead on industry-led ingredient review. It is clear that the sector has a fragmented regulatory structure with limited government monitoring and enforcement.⁵⁵

The European Union, by contrast, adopted formal regulation with clear lists of accepted, restricted, and prohibited ingredients with the passage of the Cosmetics directive in 1976. An early initiative of the internal market project, the directive aimed to guarantee the safety of these products, while facilitating the free exchange of such consumer goods within the European market. The European Commission, specifically DG Enterprise, oversees the implementation of the directive.

Over the following three decades, the EU has built its regulatory expertise and control over market access. In terms of expertise, the EU founded the European Centre for the Validation of Alternative Methods (ECVAM) in 1991. ECVAM studies alternatives to testing on animals and approves such procedures for use in the EU market. In 1997, the European Union created the Scientific Committee on Cosmetic Products (this committee became the Scientific Committee on Consumer Products (SCCP) in 2004). Comprised of experts from the member states, the committee analyzes the safety of ingredients that should be placed on the various ingredients lists. These recommendations are forwarded to the Commission, which decides which substances should be prohibited or restricted in the European market. This network of scientific experts has greatly enhanced the level of expertise available to the Commission as it reviews individual products and the Centre for alternative testing provides the Commission with critical technical information.⁵⁶

In terms of market access, successive reforms have expanded EU control. Starting with the 6th Amendment to the Cosmetics directive adopted in 1993, the EU prohibited the marketing of cosmetics that contained ingredients that had been tested on animals. It requires firms to use alternative testing methods that do not involve animal subjects. The implementation of the prohibition was delayed twice so as to allow the development of such validation procedures.

In 2003, the European Union adopted the 7th Amendment to the directive, which further enhanced European regulatory capacity. The Amendment extends the ban to include not only ingredients but also finished products that have been tested on animals and sets a final deadline for implementation of 2009. This Amendment is monitored and implemented by ECVAM with oversight and coordination by the Commission. The 7th Amendment also enhanced the consumer protection aspects of the regime. Most important, the reform significantly expanded the list of ingredients that were considered prohibited or restricted. Substances containing category 1 and 2 carcinogens were placed on the list. As a result, the number of prohibited ingredients has doubled to nearly one thousand and it has increased the types of ingredients that are analyzed by the SCCP.⁵⁷

International ramifications of European reforms

⁵⁵ See Analysts 2004.

⁵⁶ See Ibid..

⁵⁷ See Ibid..

The development of regulatory capacity has been central to the extraterritorial export of European rules. In order to facilitate this modeling, the EU has conducted capacity building exercises in other countries. The most intense of these efforts occurred between the EU and ASEAN, when the EU sent a group of technical experts to the region to help in their development of a cosmetics directive. The effect of this capacity building is seen in the text of the directive adopted by ASEAN, which incorporates both the substantive list of banned substances in Europe with institutional features of the European regulatory regime. The ASEAN directive creates an ASEAN Cosmetics Scientific Body, which has as one of its mandates the active review of developments in the European Union. Since the adoption of the ASEAN directive in 2003, experts from Brunei, Cambodia, Indonesia, Lao, Malaysia, Philippines, Singapore, Thailand, and Vietnam have traveled to Europe for Commission sponsored trainings. Minutes of the ASEAN Cosmetics Scientific Body routinely reference input from the European Commission and deference to its expertise.⁵⁸ Similar capacity building exercises have been conducted in Latin America, including meetings in Venezuela and Chile to promote its ingredient list system.

The EU has also used its regulatory capacity to control market access to shape multinational corporations behavior.⁵⁹ Many MNCs have eliminated banned substances and are exploring alternative testing regimes. In the US, the European regulations have spurred national animal rights and consumer safety lobbies to place additional pressure on cosmetics corporations. In a well-publicized dispute, the Campaign for Safe Cosmetics, a US-based coalition of consumer and environmental groups, seized on the Europe-wide ban of phthalates in cosmetics to pressure leading cosmetics firms to voluntarily ban the substance in the US also. After an aggressive advertising campaign, industry giants such as Revlon, Estée Lauder, and L'Oréal complied even though both FDA and CFTA maintained there was no evidence that the substance could potentially harm consumers.⁶⁰

While the lopsided distribution of regulatory capacity has structured international cosmetics regulation around EU dominance and extraterritorial promotion of EU rules, transgovernmental regulatory cooperation has taken hold in a specific subfield. Importantly, cooperation has succeeded in the one area where US policymakers managed to augment US regulatory capacity. In response to European efforts on alternative testing, the US established an agency to oversee the scientific certification of such techniques, the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).⁶¹ As the deadline for the first alternative-testing ban approached, regulators from four major markets – the EU, US, Japan, and Canada – sat down to resolve issues of regulatory conflict. It is interesting to note that Health Canada, which has a long tradition in regulating cosmetics, was included in the transgovernmental process. This seems to confirm the “Kissenger Effect” more than either of the other two theories as Canada is not a significant global cosmetics market. Similarly, the absence of China and Brazil (both with fledgling regulatory states) from the transgovernmental forum – labeled International Cooperation on Cosmetics

⁵⁸ See the ASEAN Cosmetics Association at <http://www.aseancosmetics.org/default>.

⁵⁹ See Stuart Sherwin, “Tea-Tree Trade Threat – EU Moves to Ban Imports,” *Courier Mail*, 3 March 2007.

⁶⁰ See Laurel Naversen Geraghty, “Should You Worry About the Chemicals in Your Makeup?,” *The New York Time*, 7 July 2005.

⁶¹ See Donnellan 2007.

Regulation – in 2007 confirms the importance of domestic regulatory capacity for potential transgovernmental cooperation. Additionally, the breakdown of previous transgovernmental cooperation in the form of the CHIC meetings supports the relative sequencing argument presented above as the FDA does not have regulatory capacity in the issue area but relies on industry self-regulation.⁶² The failure to incorporate those industry representatives no doubt contributed to slow progress in cooperation.

CONCLUSION

The global pharmaceuticals and cosmetics markets have reached \$700 billion in combined value, similar in size to the market for steel. Despite the sectors' size, their strategic importance at the intersection of manufacturing and cutting-edge, intellectual property-intensive research, and the many public health concerns tied up with the sectors' regulation, IPE scholars have paid relatively little attention to their international governance. This is mostly because existing analytic tools and theories struggle with governance that differs considerably from the conventional image of international cooperation. Instead of typical interstate treaty organizations, international governance in these markets is provided through a mix of extraterritorial extensions of national law and network-based transgovernmental cooperation – safety standards, market access rules, and other non-tariff barriers have replaced formal trade agreements as the key focus of international public policy. Governance patterns in international pharmaceutical- and cosmetics markets are not a quirky outlier. Rather, they are examples of what we call international market regulation, the set of policy challenges and policy dynamics at the heart of integrating markets.

Existing approaches encounter serious limitations when applied to international market regulation. For sure, the realist focus on market size and liberal functionalists' attention to underlying market friction and patterns of interdependence offer insights. Realists are correct in their assertion that international market regulation is usually the domain of the largest and most powerful markets. However, power cannot be reduced to market size. We find instances where smaller markets can impose their preferences on larger ones. Moreover, changes in relative market size do not correspond to shifting influence patterns within international regulatory regimes. Similarly, liberals are correct that international market regulation is driven to a large extent by interdependence resulting from cross-border market integration. Furthermore, efforts to reduce international market friction are clearly central to regulators' international agenda. But liberalism also falls short. International efforts are not necessarily initiated by the most internationally oriented market. In addition, liberalism cannot satisfactorily explain the emergence of transgovernmental cooperation alongside extraterritorial applications of national law or the changing locus of influence within international regulatory regimes.

Making sense of policy dynamics inside international market regulation requires an analysis of domestic institutional development. Globalization and market integration bring national regulatory structures that have evolved along distinct institutional trajectories into contact, and often into conflict with one another. In the ensuing political dynamics, domestic regulators must balance the defense of existing national bargains with new demands arising from globalization. Regulatory capacity is a critical variable in this respect. Advanced economies have largely abandoned Keynesian demand management and politically-motivated monetary policy. Deprived of these

⁶² Interview with the author with an industry spokesperson. Brussels, 2007.

earlier tools for economic management, governments now rely on a series of micro-institutional structures to steer market competition in different sectors. Globalization means that agencies and commissions created with an eye primarily to the domestic market are increasingly engaged in international market coordination and conflict management. But not all agencies or regulatory systems are equal. We argue that differences in the relative development of regulatory capacity – what we call sequencing – is a principal driver in changing patterns of interaction in international market regulation. Their institutional resources and capabilities vary greatly across countries, sectors, and time. And this variation profoundly shapes international market regulation.

The domestic institutional argument put forth in this article offers a corrective to existing work focused on market size or market friction and thus make an important contribution to the literature. International market regulation features a different kind of politics, one in which domestic regulatory actors take on critical international roles. Regulatory capacity explains why and when sizeable markets become a source of international influence. Similarly, it sheds light on who is likely to make the first move against the backdrop of market friction, who controls the policy agenda, and why and when extraterritorial application of national laws may give way to cooperation. To be clear, the domestic institutional argument is not deterministic; it does not predict with complete certainty what will happen in a sector given the underlying distribution of regulatory capacity. Rather, it is a probabilistic argument that highlights the critical role of domestic regulatory capacity and its sequential development for international market regulation.

Beyond correcting shortcomings of arguments stressing market size or market friction, the paper makes two important contributions to the literature on international political economy. In emphasizing the importance of sequencing and regulatory capacity, the paper sheds light on the conditions under which transgovernmental cooperation may occur. Much of the burgeoning literature on transgovernmental networks has focused on the pressures globalization has placed on the state to find new, fast and flexible governance solutions, and how such networks offer just that. Less attention has been paid to the critical question when and where transgovernmental networks are likely to appear. After all, we can only find them in a few areas and most have developed fairly recently. This study suggests that sufficient regulatory capacity in leading markets is a pre-condition for transgovernmental cooperation. Networks have to be anchored on solid domestic nodes. Persistent institutional asymmetry – the “Kissinger Effect” – makes robust transgovernmental cooperation unlikely. As regulatory state-type institutions spread across sectors and countries, we would expect transgovernmental cooperation to become more prevalent. Yet it will never completely displace conventional interstate governance because many areas of economy and society remain under direct control of governments and elected officials, rather than independent regulatory agencies.

Furthermore, the findings make an important contribution to the debate over product- and process standards in international market competition. Scharpf put forth a compelling argument that has become conventional wisdom. He urges governments to regulate domestic markets via product standards as these can more easily be linked to market access control and can thus be imposed on foreign imports. Strict product standards in large, attractive markets can set off the “trading up” dynamic identified by Vogel. In contrast, domestic process standards risk putting domestic producers at a

competitive disadvantage as these are generally hard to impose on foreign producers. The pharmaceutical and cosmetics cases show that this is not universally so. Extraterritorial application of national law works via process standards. The FDA, for example, required foreign producer to submit to the same grueling drug development and approval scheme that applied to US firms, as a condition for market access. In both cases – the US in pharmaceuticals and Europe in cosmetics – the extraterritorial application of process standards has proven an effective tool to force foreign ratcheting up of regulation. It is possible that these two cases are exceptions that prove the rule. Because of the nature of both industries, product safety is maintained via careful monitoring of the product development process. More likely, however, Scharpf's influential argument has to be conditioned. In a range of sectors, from biotechnology to high value-added professional services, product- and process regulation are closely intertwined. In cases where product safety is ensured via regulation of the production process, potent domestic regulators may in fact be able to force foreign ratcheting up via process standards. Further research should probe this proposition.

This conclusion highlights some of the intriguing areas for future inquiry. International market regulation offers an ideal terrain to drive research on the interaction of domestic and international politics forward. International market regulation unfolds transnationally, often below the radar of established international organizations and heads of government. Instead, domestic regulatory agencies are the principal protagonists. The stakes are nevertheless high as rules for multi-billion global industries affecting people all over the world take shape. We are convinced that IPE scholars will pay more attention to international market regulation and historical institutionalism offers a robust and attractive analytic toolbox for the construction of future theories.

REFERENCES

- Abbott, Kenneth W., and Duncan Snidal. 1988. Why States Act through Formal International Organizations. Journal of Conflict Resolution 42(1): 3-32.*
- Aggarwal, Vinod K. 1985. Liberal protectionism: the international politics of organized textile trade. Berkeley: University of California Press.*
- Analysts, Risk and Policy. 2004. Comparative Study on Cosmetics Legislation in the EU and Other Principal Markets with Attention to so-called Borderline Products. Norfolk, UK: Prepared for the European Commission.*
- Bach, David, and Abraham L. Newman. 2007. The European Regulatory State and Global Public Policy: Micro-Institutions, Macro-Influence. Journal of European Public Policy 14(6): 827-46.*
- Blaschke, J. 2005. Globalization of Cosmetic Regulation. Food and Drug Law Journal(60): 413-20.*
- Büthe, Tim. 2002. Taking Temporality Seriously: Modeling History and the Use of Narratives as Evidence. American Political Science Review 96(3): 481-93.*
- Carpenter, Daniel. 2001. The Forging of Bureaucratic Autonomy. Princeton, NJ: Princeton University Press.*
- DiMasi, J.A. 2001. New Drug Development in U.S. 1963-1999. Clinical Pharmacology & Therapeutics.*
- Donnellan, L. 2007. Animal Testing in Cosmetics: Recent Developments in the European Union and the United States. Animal Law(13): 251.*
- Drezner, Daniel W. 2007. All Politics is Global: Explaining International Regulatory Regimes. Princeton: Princeton University Press.*
- . 2005. *Globalization, Coercion, and Competition: The Competing Pathways to Policy Convergence. Journal of European Public Policy 12(5): 841-59.*
- Evans, Peter B., Dietrich Rueschemeyer, and Theda Skocpol, eds. 1985. Bringing the State Back In. Cambridge: Cambridge University Press.*
- FDA Reform and the European Medicines Evaluation Agency. 1995. Harvard Law Review 108(8): 2009-26.*
- Feick, Jürgen. 2002. Regulatory Europeanization, National Autonomy and Regulatory Effectiveness: Marketing Authorization of Pharmaceuticals. In Max Planck Institut Discussion Paper 02(6): Max Planck Institut.*
- Fox, Eleanor M. 1997. Toward World Antitrust and Market Access. American Journal of International Law 91(1): 1-25.*
- Frieden, Jeffrey A., and Lisa L. Martin. 2002. International Political Economy: Global and Domestic Interactions. In Political Science: State of the Discipline, edited by Ira Katznelson and Helen V. Milner, 118-46. New York: W.W. Norton.*

- Gilardi, Fabrizio. 2002. Policy credibility and delegation to independent regulatory agencies: a comparative empirical analysis. Journal of European Public Policy 9(6): 873-93.*
- Global Insight. 2007. A Study of the European Cosmetics Industry, Prepared for the European Commission. Milan.*
- Goodman, John. 1991. The Politics of Central Bank Independence. Comparative Politics 23(3): 329-49.*
- Hall, Peter A. 1986. Governing the economy: the politics of state intervention in Britain and France. New York: Oxford University Press.*
- Henney, Jane E. 2001. FDA & Globalization In The 21st Century. In Biomedical Market Newsletter.*
- IMS Health. 2004. IMS World Review. Norwalk, CT.*
- James, Scott C., and David A. Lake. 1989. The Second Face of Hegemony: Britain's Repeal of the Corn Laws and the American Walker Tariff of 1846. International Organization 43(1): 1-29.*
- Kahler, Miles, ed. forthcoming. Networked Politics: Agency, Power, and Governance.*
- Kahler, Miles, and David A. Lake, eds. 2003. Governance in a Global Economy: Political Authority in Transition. Princeton: Princeton University Press.*
- Keohane, Robert O. 1984. After hegemony: cooperation and discord in the world political economy. Princeton: Princeton University Press.*
- . 1983. *The Demand for International Regimes. In International Regimes, edited by Stephen D. Krasner, 141-72. Ithaca: Cornell University Press.*
- Kidd, D. 1996-1997. The International Conference on Harmonization of Pharmaceutical Regulation, the European Medicines Evaluation Agency, and the FDA: Who's Zooming Who. Global Legal Studies Journal(4): 182-206.*
- Knopf, Jeffrey. 1993. Beyond Two-Level Games: Domestic-International Interaction in the Intermediate-Range Nuclear Forces Negotiations. International Organization 47(4): 599-628.*
- Krasner, Stephen D. 1976. State Power and the Structure of International Trade. World Politics 28(2): 317-47.*
- Krasner, Stephen. D. 1991. Global Communications and National Power: Life on the Pareto Frontier. World Politics 43(3): 336-66.*
- Kulynych, J. 1999. Will FDA Relinquish the 'Gold Standard' for New Drug Approval? Food and Drug Law Journal 54: 127-49.*
- Lee, J. John. 2005. What is Past is Prologue: the International Conference on Harmonization and Lessons Learned from European Drug Regulations Harmonization. University of Pennsylvania Journal of International Economic Law(Spring): 151-91.*
- Lee, P. , and J. Herzstein. 1986. International Drug Regulation. Annual Review of Public Health 7: 217-35.*

- Martin, Lisa L., and Beth A. Simmons. 1998. *Theories and Empirical Studies of International Institutions*. *International Organization* 52(4): 729-57.
- Mattli, Walter, and Tim Büthe. 2003. *Setting International Standards: Technological Rationality or Primacy of Power?* *World Politics* 56(1): 1-42.
- Meunier, Sophie. 2005. *Trading Voices: The European Union in International Commercial Negotiations*. Princeton: Princeton University Press.
- Milner, Helen V. 1997. *Interests, institutions, and information: domestic politics and international relations*. Princeton: Princeton University Press.
- Molzon, Justina A. 2005. *The International Conference on Harmonization Common Technical Document - Global Submission Format?* *Food and Drug Law Journal*(60): 447-51.
- Moran, Michael. 2002. *Understanding the Regulatory State*. *British Journal of Political Science* 32(2): 391-412.
- Newman, Abraham L. 2008. *Protectors of Privacy: Regulating Personal Data in the Global Economy*. Ithaca: Cornell University Press.
- North, Douglass , and Barry Weingast. 1989. *Constitutions and Commitment: The Evolution of Institutions Governing Public Choice in Seventeenth-Century England*. *Journal of Economic History* 49(4): 803-32.
- Oh, C. H., and A. Rugman. 2006. *Regional Sales of Multinationals in the World Cosmetics Industry*. *European Management Journal* 24(2-3): 163-73.
- Pierson, Paul. 2000. *Not Just What, but When: Timing and Sequence in Political Processes*. *Studies in American Political Development* 14: 72-92.
- . 2004. *Politics in Time: History, Institutions, and Social Analysis*. Princeton: Princeton University Press.
- Pilot, Larry R. 2000. *FDA inspection of european device manufacturers and the incredible effect It has on you*. *Biomedical Market Newsletter* 10(10).
- Putnam, Robert D. 1988. *Diplomacy and Domestic Politics: The Logic of Two-Level Games*. *International Organization* 42(3): 427-60.
- Raustiala, Kal. 2002. *The Architecture of International Cooperation: Transgovernmental Networks and the Future of International Law*. *Virginia Journal of International Law* 43: 1-92.
- . 1997. *Domestic Institutions and International Regulatory Cooperation: Comparative Responses to the Convention on Biological Diversity*. *World Politics* 49(4): 428-509.
- Richards, John E. 1999. *Toward a Positive Theory of International Institutions: Regulating International Aviation Markets*. *International Organization* 53(1): 1-37.
- Shambaugh, George E. 1996. *Dominance, Dependence, and Political Power: Tethering technology in the 1980s and today*. *International Studies Quarterly* 40(4): 559-88.
- Simmons, Beth A. 2001. *The International Politics of Harmonization: The Case of Capital Market Regulation*. *International Organization* 55(3): 589-620.

- Skowronek, Stephen. 1982. Building a new American state: the expansion of national administrative capacities, 1877-1920. Cambridge: Cambridge University Press.*
- Slaughter, Anne-Marie. 2004. A New World Order. Princeton: Princeton University Press.*
- . 1997. *The Real New World Order*. *Foreign Affairs* 76: 183-97.
- Spar, Debora L. 2001. Ruling the waves: cycles of discovery, chaos, and wealth from compass to the Internet. New York: Harcourt.*
- Thelen, Kathleen. 2004. How Institutions Evolve: The Political Economy of Skills in Germany, Britain, the United States and Japan. Cambridge: Cambridge University Press.*
- Vogal, D. 1998. The Globalization of Pharmaceutical Regulation. Governance* 11(1): 1-22.
- Vogel, David, and Robert A. Kagan. 2004. Dynamics of Regulatory Change: How Globalization Affects National Regulatory Policies. Berkeley: University of California Press.*
- Vogel, Steven K. 1996. Freer Markets, More Rules: Regulatory Reform in Advanced Industrial Countries. Ithaca: Cornell University Press.*
- Wiktorowicz, M. 2003. Emergent Patterns in the Regulation of Pharmaceuticals: Institutions and Interests in the United States, Canada, Britain, and France. Journal of Health Politics, Policy, and Law* 28(4): 615-58.
- The World Medicines Situation. 2004. Geneva: World Health Organization.*
- Zysman, John. 1983. Governments, markets, and growth: financial systems and the politics of industrial change. Ithaca: Cornell University Press.*
- . 1994. *How institutions create historically rooted trajectories of growth*. *Industrial and Corporate Change* 3(1): 243-83.

NOTAS

NOTAS
