

# Oy Canada! Trade's Non-solution to “*the* Problem” of U.S. Drug Prices

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HORSTMAN: Mr. President, why did you block the reimportation of safer and inexpensive drugs from Canada which would have cut 40 to 60 percent off of the cost?

BUSH: I haven't yet. Just want to make sure they're safe. When a drug comes in from Canada, I want to make sure it cures you and doesn't kill you.

KERRY: John, you heard the president just say that he thought he might try to be for it. Four years ago, right here in this forum, he was asked the same question: Can't people be able to import drugs from Canada? You know what he said? “I think that makes sense. I think that's a good idea” -- four years ago. Now, the president said, “I'm not blocking that.” Ladies and gentlemen, the president just didn't level with you right now again. He did block it, because we passed it in the United States Senate. We sent it over to the House, that you could import drugs. We took care of the safety issues. We're not talking about third-world drugs. We're talking about drugs made right here in the United States of America that have American brand names on them and American bottles. And we're asking to be able to allow you to get them.<sup>1</sup>

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<sup>1</sup> President George W. Bush & Senator John Kerry, Second Presidential Debate (Oct. 8, 2004) (transcript available at Commission on Presidential Debates, <http://www.debates.org/pages/trans2004c.html> (last visited April 10, 2006)) [hereinafter Second Bush-Kerry Debate]. The subject of importing drugs from Canada was revisited by Senator Kerry in the third presidential debate. See Senator John Kerry, Third Presidential Debate (Oct. 13, 2004) (transcript available at Commission on Presidential Debates, <http://www.debates.org/pages/trans2004d.html> (last visited April 10, 2006)) [hereinafter Third Bush-Kerry Debate]. To some extent, these positions run counter to partisan stereotypes. We see here, among other things, a liberal Democrat advocating for enabling Americans to opt out of certain

## I. INTRODUCTION

This bit of recent political history is ideal in this regard, if no other: It vividly encapsulates a public dispute considered important at the time of the campaign and—at least thus far—throughout the presidential term at issue in that campaign. Thus, we begin with a parochial perspective on one corner of United States (U.S.) international trade policy; that is, many U.S. citizens would prefer to import, or “re-import,” their prescription pharmaceuticals from Canada, although such importation is not permitted under federal law.<sup>2</sup> Because the federal law in question was duly enacted pursuant to the powers granted the federal Congress under the Commerce Clause of the U.S. Constitution, the federal ban preempts any putative state law statutes and regulations to the contrary.<sup>3</sup>

The fact that such cross-border trade is prohibited has been a source of ample public controversy on both sides of the U.S./Canada border. Within the United States, a widespread perception of cross-border price disparities is discussed frequently and prominently in the national press;<sup>4</sup> it is debated in our presidential campaigns;<sup>5</sup> and it is an ongoing source of federal and state legislative activity.<sup>6</sup>

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putatively inefficient federal regulatory strictures while a conservative Republican President advocates regulatory caution before expanded market choices.

<sup>2</sup> See, e.g., Pam Belluck, *Boldly Crossing the Line for Cheaper Drugs*, N.Y. TIMES, Dec. 11, 2003, at A38; Marc Kaufman, *Illinois Governor Launching Program to Reimport Drugs: Move May Force FDA's Hand*, WASH. POST, Aug. 17, 2004, at A13 (regarding state government engineered importation schemes). The ways in which such importation may run afoul of federal law are diverse and call, at least in certain instances, for substantial analysis. Briefly, drug products imported from Canada (or any other nation) are liable to run afoul of federal Food, Drug, and Cosmetic Act (FDCA) provisions regarding traffic in unapproved new drugs and/or traffic in drugs that are improperly labeled (“misbranded”). See also 21 U.S.C. § 355 (2000) and 21 U.S.C. §§ 352, 353 (2000), respectively. In addition, the FDCA provides that, generally, only a drug’s original manufacturer may return a U.S. manufactured drug to U.S. soil once that drug has been shipped abroad. 21 U.S.C.A. § 381(d)(1) (West Supp. 2005).

<sup>3</sup> See *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 348 (2001) (state-law fraud-on-the-FDA claims would conflict with FDA’s performance of its statutory responsibilities and regulatory objectives); *Fid. Fed. Sav. & Loan Ass’n v. de la Cuesta*, 458 U.S. 141, 153 (1982) (preemption of state law that conflicts with the exercise of federal power, including regulatory power); *Walsh v. U.S.*, 331 U.S. 432, 434 (1947) (the 1938 Federal Food, Drug, and Cosmetic Act “rests upon the constitutional power resident in Congress to regulate interstate commerce ... [and] seeks to keep interstate channels free from deleterious, adulterated and misbranded articles of the specified types.”). This is, of course, the barest sketch of a federalism analysis, as it might be applied to the motley of State schemes at issue. Twenty-two states have considered importation or re-importation legislation in 2005. The National Conference of State Legislatures, 2005 Prescription Drug State Legislation, <http://www.ncsl.org/programs/health/drugdisc05.htm> (last visited April 10, 2006) (summarizing information on such legislation).

<sup>4</sup> See, e.g., Joel Baglole, *Getting the Gray Out: Canadian and U.S. Regulators Are Looking to Impose Order on the Sale of Cheap Online Drugs*, WALL ST. J., Feb. 11, 2003, at R6; Belluck, *supra* note 2, at A38; Kaufman, *supra* note 2 at A13; Michael S. Rosenwald, *Merck to Discount Drugs for Uninsured: Prices to Compare to Canadian Imports*, WASH. POST, Apr. 20, 2005, at E2; Kelly K. Spors, *Canadian Drugs Are Getting Cheaper: Online Pharmacies Catering to Americans Cut Costs by Finding New Suppliers*, WALL. ST. J., July 22, 2004, at D1; Bob Tedeschi, *E-Commerce; As the Debate Continues, Opinions Are Divided over the Merits of Allowing Online Drug Purchases from Canada*, N.Y. TIMES, Mar. 8, 2004, at C4.

<sup>5</sup> See, e.g., Second Bush-Kerry Debate, *supra* note 1; Third Bush-Kerry Debate, *supra* note 1.  
<sup>6</sup> See, e.g., Ceci Connolly, *GOP Spars Over Drug Import Bill Some Senators Aim To Regulate Purchase*, WASH. POST, Apr. 20, 2005, at A23 (debate within GOP regarding merits of importation legislation). See also 21 U.S.C.A. § 384(b) (West Supp. 2005) (authorizing the promulgation of regulations for the importation of drugs from Canada; 21 U.S.C.A. §384(l) (West Supp. 2005)(stipulating that the authorization is effective only if the Secretary of HHS certifies, e.g., that re-importation poses no additional risk to American consumers). The history of federal legislation regarding Canadian importation, together with attempts by certain States to import – or

Indeed, Congressional consideration of—and qualified support for—certain forms of parallel trade in pharmaceuticals has become the Bill that will not die (or live either). Congress, across two presidential administrations, has repeatedly authorized certain drug re-importation schema, *contingent* on the approval of the U.S. federal Food and Drug Administration (FDA).<sup>7</sup> FDA has not, as yet, granted such approval, and one may wonder about the extent to which FDA stinginess in that regard has—or has not—come as a surprise to Congress.<sup>8</sup> The topic has been similarly controversial in Canada, albeit for somewhat different reasons.<sup>9</sup>

Within the United States, the debate typically is cast as President Bush and Senator Kerry cast it; that is, as a risk management problem of safety versus cost, with substantial disagreement about the accounting particulars of the fundamental variables.<sup>10</sup> In that regard, the puzzle is, as one subcommittee of Congress succinctly put it: “Are Americans being protected or gouged?”<sup>11</sup> The question appears simple, although on its face are complex technical issues of drug safety, as well as questions about regulatory integrity, competing (pharmaceutical) market systems, and equity in international trade policy. Not far beneath the surface are questions about the scope of the intellectual property (IP) protections afforded to pharmaceuticals, as the most significant price disparities are observed with respect to certain patent-protected drugs or drugs afforded some other measure of exclusivity in the market.<sup>12</sup>

What drug re-importation advocates propose is a special case of “parallel trade.” Parallel trade is simply the lawful movement of goods across international borders independent of the consent of the manufacturers of those goods and independent of

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permit the importation of – prescription pharmaceuticals will be discussed more fully in Section II, *infra*. See also S.B. 410, §§ 36-43, 79<sup>th</sup> Leg. (Tex. 2005) (authorizing Texas State Board of Pharmacy to approve Canadian pharmacies for Texas drug importation and requiring information posted for State residents on web site); S. 49 2005-6 Gen. Aseem. (Vt. 2005) (authorizing Vermont to join multi-state importation plan); National Conference of State Legislatures, *supra* note 3.

<sup>7</sup> See *infra* text accompanying notes 46-47 (regarding the Medicare, Prescription Drug Improvement and Modernization Act of 2003).

<sup>8</sup> Secretary Thompson explicitly rejected the prospect of such a certification in 2001 and current HHS Secretary Leavitt has not, thus far, suggested that he intends to reverse the course charted by his predecessor. See Robert Pear, *In a Turnaround, White House Kills Drug-Import Plan*, N.Y. TIMES, Dec. 27, 2000, at A1 (describing Dep’t of Health and Human Serv. Sec. Donna Shalala’s letter to President Clinton on Dec. 26, 2000); Letter from Tommy Thompson, Secretary, Dep’t of Health and Human Serv., to Senator James Jeffords, (July 9, 2001), available at <http://www.fda.gov/oc/po/thompson/medsact.html>.

<sup>9</sup> Canada, plainly, has been concerned that open trade with the United States might threaten the Canadian drug supply, Canadian pricing, or both. See, e.g., Reuters, *Canada Seeks to Control Sales of Drugs to U.S.: Health Minister Aims to Protect Domestic Supply*, MSNBC NEWS, June 29, 2005, <http://msnbc.msn.com/id/8406928/> (reporting on draft legislation in the Canadian parliament aimed at protecting Canadian drug supplies by prohibiting bulk exportation to the U.S.).

<sup>10</sup> See Second Bush-Kerry Debate, *supra* note 1; Third Bush-Kerry Debate, *supra* note 1.

<sup>11</sup> *International Prescription Drug Parity: Are Americans Being Protected or Gouged?: Hearing Before the Subcomm. on Human Rights & Wellness of the H. Comm. on Govt. Reform*, 108th Cong. 1 (2003), available at [http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108\\_house\\_hearings&docid=f:87228.pdf](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_house_hearings&docid=f:87228.pdf).

<sup>12</sup> See, e.g., PATRICIA M. DANZON, PRICE COMPARISONS FOR PHARMACEUTICALS: A REVIEW OF U.S. AND CROSS-NATIONAL STUDIES 28, 33-34 (1999), available at <http://hc.wharton.upenn.edu/danzon/PDF%20Files/AEI%20Price%20Comparisons%20for%20Pharmaceuticals%201999.pdf>; Patricia M. Danzon & Michael F. Furukawa, *Prices and Availability of Pharmaceuticals: Evidence from Nine Countries*, HEALTH AFFAIRS, at W3-521, Oct. 29, 2003, <http://content.healthaffairs.org/cgi/reprint/hlthaff.w3.521v1>. Drug products may be afforded significant Intellectual Property protections beyond those insured by patent and trademark rights. See *infra* text accompanying notes 65-68.

distribution channels established by those manufacturers.<sup>13</sup> Parallel trade depends on both significant cross-border price disparities and the absence of statutory and regulatory impediments to the free flow of goods.<sup>14</sup> In the case of pharmaceuticals, we have the first, but not the second. The retail prices of certain prescription drugs are lower in Canada than they are in the United States, especially for certain drugs and certain purchasers.<sup>15</sup> Because of legal barriers to trade, however, prescription drugs do not flow freely across the border and arbitrage between the two markets is constrained, albeit continuing.<sup>16</sup>

Beyond the particular U.S./Canada discussion have been controversy and concerns about a complex of issues with regard to parallel trade in pharmaceuticals generally. Some of these have focused on the possibility of parallel trade between the U.S. and broader international markets.<sup>17</sup> Some have focused on parallel trade within and without the European Union.<sup>18</sup> Finally, many have been concerned with particular issues raised by the health and economic challenges of the developing world; in particular, there has been substantial attention paid to IP protection, trade policy, and differential pricing as they bear on the Malaria and HIV/AIDS crises in sub-Saharan Africa.<sup>19</sup> Underlying these broader discussions are not just the familiar themes of equitable pricing and regulatory safety, but the question of whether competing IP regimes for pharmaceuticals imply a fundamental tradeoff between

<sup>13</sup> See, e.g., European Commission's Directorate-General for Competition, Glossary, [http://europa.eu.int/comm/competition/general\\_info/p\\_en.html](http://europa.eu.int/comm/competition/general_info/p_en.html) (last visited Apr. 10, 2006).

<sup>14</sup> See, e.g., Belinda Isaac, *The Free Movement of Goods II: Pharmaceuticals, Trade Marks, and Parallel Imports* in W.R. CORNISH ET AL., PHARMACEUTICAL MEDICINE, BIOTECHNOLOGY, AND EUROPEAN LAW 25, 29-32 (Richard Goldberg & Julian Lonbay eds., 2000).

<sup>15</sup> Which products are less expensive, by how much, and under what conditions, is a more complex matter than the public debate has allowed. See, e.g., Danzon, *supra* note 12, at 2 ("[M]inority Staff Reports are based on flawed methodology that leads to seriously upward-biased estimates of the price differences between sectors within the United States and between the United States and Canada or Mexico."); Danzon & Furukawa, *supra* note 12, at W3-522 (noting that U.S.-foreign price differentials are roughly in line with income and smaller for drugs than for other medical services.)

<sup>16</sup> Although trade barriers between the U.S. and Canada under the terms of the North American Free Trade Agreement (NAFTA), are, generally speaking, few, provisions for trade in pharmaceuticals and biotech products have not, as of the time of this writing, been incorporated in that treaty. See North American Free Trade Agreement, U.S.-Can.-Mex., Dec. 17, 1992, 32 I.L.M. 289 (Parts 1-3), 32 I.L.M. 605 (Parts 4-8).

<sup>17</sup> See, e.g., ROGER PILON, DRUG REIMPORTATION: THE FREE MARKET SOLUTION: CATO INSTITUTE POLICY ANALYSIS 521 11 (2004), *available at* [http://www.cato.org/pub\\_display.php?pub\\_id=2305](http://www.cato.org/pub_display.php?pub_id=2305) (ban on reimportation should be lifted to discourage free-riding).

<sup>18</sup> Generally speaking, parallel trade in pharmaceuticals is permitted within the European Union whereas parallel trade between member states and non-member states is not. See W.R. CORNISH ET AL., PHARMACEUTICAL MEDICINE, BIOTECHNOLOGY, AND EUROPEAN LAW (Richard Goldberg & Julian Lonbay eds., 2000) (providing a broad overview of European Union issues).

<sup>19</sup> See, e.g., COMM. ON THE ECONOMICS OF ANTIMALARIAL DRUGS, BOARD ON GLOBAL HEALTH, INSTITUTE OF MEDICINE, SAVING LIVES, BUYING TIME: ECONOMICS OF MALARIA DRUGS IN AN AGE OF RESISTANCE (Kenneth J. Arrow et al. eds., 2004), *available at* <http://www.nap.edu/books/0309092183/html>; WORLD HEALTH ORG. COMM. ON MACROECONOMICS AND HEALTH, REPORT OF WORKING GRP. 4, HEALTH & THE INT'L ECONOMY (2002); Maria Neira, Experience With Access to Essential Medicines for Tropical Diseases, World Health Organization, WHO-WTO Workshop in Differential Pricing and Financing of Essential Drugs, Høsbjør, Nor. (Apr. 2001), *available at* [http://www.wto.org/english/tratop\\_e/trips\\_e/hosbjor\\_presentations\\_e/20a\\_neira\\_e.pdf](http://www.wto.org/english/tratop_e/trips_e/hosbjor_presentations_e/20a_neira_e.pdf); Dorothy Ochola et al., Uganda HIV/AIDS Drugs Access Initiative: Current Experience with Differential Pricing of HIV/AIDS related Drugs in Uganda, World Health Organization, WHO-WTO Workshop in Differential Pricing and Financing of Essential Drugs, Høsbjør, Nor. (Apr. 2001), *available at* [http://www.wto.org/english/tratop\\_e/trips\\_e/hosbjor\\_presentations\\_e/19ochola\\_e.pdf](http://www.wto.org/english/tratop_e/trips_e/hosbjor_presentations_e/19ochola_e.pdf).

present price competition and the possibility (or rate) of innovation; that is, among other things, a balancing of present and future welfare.<sup>20</sup>

Plainly, a complete discussion of such issues and their interrelationships is beyond the scope of any one paper—hence, our beginning with a relatively local corner of the debate. Recently, important questions have been raised about whether, or to what extent, relevant national or international policies might be optimized.<sup>21</sup> Suggested in this paper—but argued elsewhere—is that no clear, general solution to the optimization problem is likely forthcoming.<sup>22</sup> I suppose that, the more fundamental problems seen in, e.g., attempts to rationalize antitrust and IP policy remain, only to be amplified as we account for problems of trade, regulatory, and international health policy as well.<sup>23</sup> Thus, optimizing the balance between IP and Antitrust doctrine becomes more difficult still as the matrix of legal, economic, and institutional considerations expands to fit our price discrimination problem.<sup>24</sup>

Leaving aside the problem of a general solution, my overarching goals in this paper are two. First, I shall argue that various Canada-focused re-importation

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<sup>20</sup> See, e.g., W.R. Cornish, *The Free Movement of Goods I: Pharmaceuticals, Patents and Parallel Trade*, in PHARMACEUTICAL MEDICINE, BIOTECHNOLOGY, AND EUROPEAN LAW 11, 24 (Richard Goldberg & Julian Lonbay eds., 2000) (the effect of patents as incentives to innovate is enhanced if patentees can engage in international price discrimination); Patricia M. Danzon & Adrian Towse, *Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents*, 3 INT'L J. HEALTH CARE FIN. & ECON. 183 (2003) (differential pricing, based on Ramsey pricing principles, is the second best efficient means of paying for the global joint costs of pharmaceutical R&D); Stephen Latham, *Pharmaceutical Costs: An Overview and Analysis of Legal and Policy Responses by the States*, 24 J. LEGAL MED. 141, 173 (2003) (our present goal of establishing or maintaining low drug prices is in fundamental tension with our long-term goal of developing new treatments and distributing them to a growing, and increasingly long-lived, population); WORLD HEALTH ORG. COMM. ON MACROECONOMICS AND HEALTH, *supra* note 19, at 41 (regarding “struggle” to balance static and dynamic efficiency in price differentiation). *But c.f.*, Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 YALE J. HEALTH POL'Y L. & ETHICS 193, 222 (2005) (arbitrage between high income markets may not damage innovation and the burden of proof for IP rights and barriers to parallel trade lies with the pharmaceuticals industry).

<sup>21</sup> Danzon & Towse, *supra* note 20, at 184 (differential pricing, based on Ramsey pricing principles, is the second best efficient means of paying for the global joint costs of pharmaceutical R&D and would also be consistent with standard norms of equity); Daniel J. Gifford, *How Do the Social Benefits and Costs of the Patent System Stack up in Pharmaceuticals?*, 12 J. INTELL. PROP. L. 75, 112 (2004) (patent term may be supra-optimal for some pharmaceuticals); Outterson, *supra* note 20, at 196 (applying the “heuristic device of optimal pharmaceutical rents”) (emphasis added).

<sup>22</sup> Daniel Gilman, *Something Shy—Perhaps Far Shy—of Optimization: Reconciling Price, Property, Trade, and Trust for Medicines on a Global Stage* (unpublished manuscript, on file with author). See also *infra* note 24, regarding some of the themes of that discussion.

<sup>23</sup> See Louis Kaplow, *The Patent-Antitrust Intersection: A Reappraisal*, 97 HARV. L. REV. 1813, 1815 (1984) (expressing pessimism about the prospects of determining an optimal patent term and an optimal balance of patent and anti-trust policy).

<sup>24</sup> See *id.* at 1848. Kaplow's skepticism about an optimal, joint patent-anti-trust policy is borne of what might be seen as theoretical, technical, and institutional concerns. Although an industry-specific focus may diminish a few of the problems he raises, it may just as easily amplify others. Here, we are concerned about an exploding complexity in the problem space when we seek to optimize across more, rather than fewer, bodies of law, and as we expand the types of institutions and legal systems implicated across these subjects on an international stage. Indeed, optimizing the fundamental tradeoff within IP policy itself is liable to be, to some extent, arbitrary. The value of any particular innovation is a highly contingent matter, of course, hanging on diverse properties of the market and the strategic action, or inaction, of competitors. At the same time, problem solving—within the domain of pharmaceutical development more generally—is not likely a natural kind and not likely to covary in any straightforward fashion with the resources placed at its disposal. If we suppose, further, that diverse economies may model diverse discount rates, we confound further the hope of a systematic balancing of the costs and benefits entailed by any particular IP policy.

schemes are not likely worth the candle. That is so not because Canadian drug regulation is radically inferior to U.S. drug regulation—or even radically different from it—but because there are substantial costs to dissolving the regulatory border between the two nations with relatively little to be gained in doing so. In brief, there are regulatory costs because: drugs are beneficial products but risky ones; regulation is a way of managing those risks, not a way of eliminating them; and parallel trade confounds the regulatory task. Without substantial administrative oversight, parallel trade in drugs is dangerous.<sup>25</sup> That substantial administrative task is not cost-justified because, whatever we *might* wish to do to control drug prices, it is extremely unlikely that we can do much at all by integrating the U.S. and Canadian markets.<sup>26</sup>

Second, I will consider some of the costs of administration as they may apply to parallel trade in pharmaceuticals more generally. Advocates of parallel trade with Canada may argue that the U.S. and Canada provide a special case of regulatory convergence, or the *de facto* harmonization of two regulatory systems. When we consider regulatory harmonization more broadly however, we need to consider not just the benefits to be had from streamlined regulations but the costs implied in administering them. I suggest that harmonization may impose special agency costs beyond those typical of bureaucratic administration, costs that may come to swamp what may be seen as efficiencies of regulatory production.<sup>27</sup> I consider, then, European harmonization as it appears to model some of the costs, benefits, and difficulties of regulatory integration more generally. We would do well to observe these phenomena but not—at present—to import them.

## II. LEGAL AND ECONOMIC BACKGROUND

### A. CONSTRUCTING THE REGULATORY BORDER

The borders of the United States are, among other things, expressions of its sovereignty. The borders of Canada are, similarly, expressions of its sovereignty. Concomitant with that sovereignty, and constrained by various international agreements, each nation controls the flow of goods across its borders, however imperfect the exercise of that control may be.<sup>28</sup> That boundary is not, in itself, an

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<sup>25</sup> Of course, not all risk management endeavors are efficient or even beneficial. The general argument, developed below, is that pharmaceuticals markets are especially good candidates for regulation. *See generally* R.H. Coase, *The Problem of Social Cost*, 3 J. L. & ECON. 1 (1960) (regarding social costs amenable to administrative management).

<sup>26</sup> Pessimism about the efficacy of parallel trade as a price management tool, independent of questions regarding its larger costs, has been expressed elsewhere. *See, e.g.*, CONG. BUDGET OFFICE, WOULD PRESCRIPTION DRUG IMPORTATION REDUCE U.S. DRUG SPENDING?, ECONOMIC BUDGET ISSUES BRIEF *passim* (Apr. 29, 2004), available at <http://www.cbo.gov/ftpdocs/54xx/doc5406/04-29-PrescriptionDrugs.pdf>. We may also wonder about the extent to which we *ought* to manage those prices, since the legally protected market power that permits the pricing is the fundamental inducement to innovation in the industry.

<sup>27</sup> For a general definition of agency costs, *see, e.g.*, Michael C. Jensen & William H. Meckling, *Theory of the Firm: Managerial Behavior, Agency Costs, and Ownership Structure*, in FOUNDATIONS OF CORPORATE LAW 7, 7-12 (Roberta Romano ed., 1993).

<sup>28</sup> The demarcation of the shared border between the United States and Canada has its roots in the Treaty of Paris of 1783, which, not incidentally, brought a formal end to the American Revolutionary War. *See* The Treaty of Paris, U.S.-U.K., art 2, Sept. 3, 1783, 8 Stat. 80. The International Boundary Commission, charged with surveying and mapping that boundary, was established by the Jay Treaty of 1794. International Boundary Commission, <http://www.internationalboundarycommission.org/ibcpg2.htm> (follow “Boundary History” hyperlink)

obstacle to parallel trade in pharmaceuticals across it. As a general matter, trade across the boundary is governed by various international agreements, chief among them being agreements aimed at the furtherance of free trade, not its suppression. The General Agreement on Tariffs and Trade (GATT), and subsequent Uruguay Round Agreements, of which the U.S. and Canada are both signatories, nonetheless provide WTO member nations with considerable latitude in maintaining various regulatory standards regarding, e.g., health and environmental protections, despite the fact that such standards may impede trade.<sup>29</sup> The North American Free Trade Agreement (NAFTA), a central objective of which is to eliminate non-tariff barriers to trade, also preserves the ability of signatories to maintain health and safety standards.<sup>30</sup> The central impediments, in this matter, are not the political boundary between the two countries or any positive agreement between them.<sup>31</sup> Rather, the impediments are to be found in specific statutory provisions on either side of the border and, especially, in their regulatory implementation.<sup>32</sup>

The regulation by FDA of prescription drugs, among other products, is well established.<sup>33</sup> As a general matter, the federal Food, Drug, and Cosmetic Act

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(last visited Apr. 2, 2006) (containing information on the Commission and the border). Further refinements to the boundary have been recognized in the centuries since, and certain limited particulars remain contested. *See id.*

<sup>29</sup> General Agreement on Tariffs and Trade (GATT), pt. 5, March 24, 1948, 61 Stat., 55 U.N.T.S. 194. Although GATT provided rules governing a considerable portion of world trade from its inception, it was, until 1995, essentially a provisional agreement. Most formal requirements related to the GATT arose from the World Trade Organization's (WTO's) Uruguay Round negotiations, conducted from 1986-1994, and signed at the Marrakesh Ministerial Meeting in April 1994. Final Act Embodying the Results of the Uruguay Round of Multilateral Trade Negotiations, April 15, 1994, April 15, 1994, 1867 U.N.T.S. 14. The Uruguay Round's Agreement on Technical Barriers to Trade, for example, recognizes that countries have the right to establish protection, at levels they consider appropriate, for example for human, animal or plant life or health or the environment, and should not be prevented from taking measures necessary to ensure those levels of protection are met. *Id.* at 1868 U.N.T.S. 120. WTO legal texts and summaries are maintained at World Trade Organization, [http://www.wto.org/english/docs\\_e/legal\\_e/legal\\_e.htm](http://www.wto.org/english/docs_e/legal_e/legal_e.htm) (last visited Dec. 2, 2005).

<sup>30</sup> *See* North American Free Trade Agreement (NAFTA), *supra* note 16, 32 I.L.M. at 387:

Each Party may, in accordance with this Agreement, adopt, maintain or apply any standards-related measure, including any such measure relating to safety, the protection of human ... life or health... and any measure to ensure its enforcement or implementation. Such measures include those to prohibit the importation of a good of another Party ... that fails to comply with the applicable requirements of those measures or to complete the Party's approval procedures.

For a general discussion of the implication of NAFTA for pharmaceuticals, *see* Lars Noah, *NAFTA's Impact on the Trade in Pharmaceuticals*, 33 HOUS. L. REV. 1293 (1997).

<sup>31</sup> There are, of course, economic costs associated with importation and exportation across a regulated (and policed) border that are the product of positive agreements regarding, e.g., customs operations at the border crossings themselves, which impose costs above transportation costs narrowly construed.

<sup>32</sup> On the U.S. side, regulatory authority over different aspects of the border is distributed. Of central interest generally are the Department of Homeland Security, the Department of the Treasury, the Department of State, and the Office of the United States Trade Representative. The boundary itself is charted and maintained jointly, by the International Boundary Commission (the U.S. Commissioner of which reports to the Secretary of State, while the Canadian Commissioner is located within the Department of Natural Resources Canada). *See* International Boundary Commission, <http://www.internationalboundarycommission.org/ibcpg2.htm> (last visited Apr. 2, 2006). For our particular purposes, the role of the FDA in establishing the legal boundary for trade in prescription drugs is central.

<sup>33</sup> *See* U.S. v. Walsh, 331 U.S. 432, 434 (1947) (the 1938 Federal Food, Drug, and Cosmetic Act "rests upon the constitutional power resident in Congress to regulate interstate commerce ... [and]

(“FDCA” or “the Act”) vests the authority to promulgate regulations under the Act in the Secretary of the U.S. Department of Health and Human Services (HHS).<sup>34</sup> By regulation, that authority is delegated to the Commissioner of the FDA.<sup>35</sup> Regarding the importation of drugs, the Act assigns authority jointly to the Secretary of HHS and the Secretary of the Treasury.<sup>36</sup>

The ways in which such importation may run afoul of federal law are diverse. Briefly, drug products imported from Canada (or any other nation) likely violate FDCA provisions regarding the trafficking of unapproved new drugs, adulterated drugs, and/or “misbranded” (improperly labeled) drugs.<sup>37</sup> As a statutory matter, these categories of prohibited products are interrelated.<sup>38</sup> As a policy matter, FDA has long viewed, e.g., drug safety and drug labeling as inextricably linked.<sup>39</sup> In brief, drugs are more-or-less safe, and more-or-less effective, *in context*, and the relevant context has a great deal to do with the information surrounding a drug. Drugs may be reasonably safe and efficacious for certain indicated uses, in certain populations, at certain dosage, according to certain administration, and acknowledging certain precautions, warnings, contraindications, and possible adverse events.<sup>40</sup> They function and are regulated not just as chemical entities, but as chemical entities conceived and applied *under particular descriptions*.<sup>41</sup>

Contamination or other physical degradation of drug products, in transit or storage, may render them “adulterated” under the act.<sup>42</sup> In addition, because the Act prohibits interstate commerce in any drug not generally recognized “as safe and effective for use under the conditions prescribed, recommended, or suggested *in the labeling thereof*,” such changes in an existing product may run afoul of provisions regarding unapproved new drugs.<sup>43</sup> Counterfeit products may be similarly in conflict with the Act. Labeling or dosage changes made specifically to suit the Canadian market, may render a product “misbranded” or an unapproved “new drug.”<sup>44</sup> Finally, the FDCA provides that, generally, only a drug’s original

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seeks to keep interstate channels free from deleterious, adulterated, and misbranded articles of the specified types.”)

<sup>34</sup> See 21 U.S.C. § 371(a) (authority to promulgate regulations vested in the Secretary).

<sup>35</sup> See 21 C.F.R. § 10.40(a) (2005).

<sup>36</sup> See 21 U.S.C. § 381.

<sup>37</sup> See 21 U.S.C. §§ 355 (a), 351, and 352, 353 (regarding new, adulterated, and misbranded drugs respectively), 21 U.S.C. § 355 (a) (prohibiting the introduction or delivery for introduction into interstate commerce of any unapproved new drug), and 21 U.S.C. § 331(a) (prohibiting “the introduction or delivery for introduction into interstate commerce of any ... drug ... that is adulterated or misbranded).

<sup>38</sup> For example, a drug is adulterated if, among other things, it fails to have the safety, strength, quality, and purity it “purports or is represented to possess.” See 21 U.S.C. § 351(a)(2)(B) (emphasis added). A drug is “misbranded” if its labeling is “false or misleading in any particular.” See 21 U.S.C. § 352(a). A new drug is any drug not generally recognized “as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof.” See 21 U.S.C. § 321(p).

<sup>39</sup> New Drug and Antibiotic Regulations, 50 Fed. Reg. 7452, 7470 (Feb. 22, 1985) (“Drug labeling serves as the standard under which FDA determines whether a product is safe and effective.”) FDA regulates all such labeling, including “all written, printed, or graphic matter” marketing the drug. 21 C.F.R. § 1.3(a).

<sup>40</sup> See 21 C.F.R. §§ 201.5, 201.56-7 (2005).

<sup>41</sup> See New Drug and Antibiotic Regulations, *supra* note 39.

<sup>42</sup> A drug may become adulterated should mishandling cause it to fail to have the strength, quality, or purity it purports to have in its labeling. See 21 U.S.C. § 351(a).

<sup>43</sup> See 21 U.S.C. §§ 321(p), 351(a), 355(a).

<sup>44</sup> See 21 U.S.C. §§ 351(a), 352(a).

manufacturer may return a U.S. manufactured drug to U.S. soil once that drug has been shipped abroad.<sup>45</sup>

The Medicare, Prescription Drug Improvement and Modernization Act of 2003 does provide for the promulgation of regulations to permit pharmacists and wholesalers to import prescription drugs into the U.S. from Canada.<sup>46</sup> At the same time, that section of the FDCA was drafted to provide the Secretary with a suicide brake on precisely the activity the section contemplates: The importation section itself states that it “shall become effective only if the Secretary certifies to the Congress that the implementation of this section will--(A) pose no additional risk to the public's health and safety; and (B) result in a significant reduction in the cost of covered products to the American consumer.”<sup>47</sup>

Read strictly, the conditions required by subsection 804(l) would be extremely difficult, if not impossible, to meet.<sup>48</sup> Then-Secretary Thompson explicitly rejected the prospect of such a certification in 2001 and Secretary Leavitt has not, thus far, suggested that he intends to reverse the course charted by his predecessor.<sup>49</sup> An earlier statutory provision—also authorizing the Secretary to promulgate regulations for an importation scheme, contingent on the Secretary's own assessment of the scheme's safety, was rejected by HHS Secretary Donna Shalala.<sup>50</sup> In effect, the Congress has assigned to FDA—via statute and regulatory delegation—the very possibility of drug importation, and not just its administration. As a result, the importation (or re-importation) of U.S. manufactured drugs into the United States, whether by a private U.S. citizen, a Canadian citizen, or a State or Provincial government is liable to be in violation of the FDCA—in violation at least of Section 801 of the Act and very likely in violation of one of the provisions of Section 301 or Section 505 as well.<sup>51</sup>

State legislatures have been nonetheless active in considering, or attempting to implement, the importation of prescription pharmaceuticals. Twenty-two states

<sup>45</sup> See 21 U.S.C. § 381(d)(1).

<sup>46</sup> See 21 U.S.C. § 384(b) (Supp. I 2005).

<sup>47</sup> 21 U.S.C. § 384(l).

<sup>48</sup> The question posed in the Second Bush-Kerry debate seems to suggest that U.S.-approved and manufactured drugs are not only cheaper, once transported to Canada, but safer. See Second Bush Kerry Debate, *supra* note 1. That is dubious, if not incoherent. Drug products generally cannot become safer via increasingly complex distribution pathways and increasingly long time in transport, except to the extent that product degradation may serve to reduce both therapeutic efficacy and side effects. An argument has been made that certain importation schemes, by simplifying packaging options and possible distribution complexities in the U.S. market, will “dramatically” reduce medication errors and the risk of counterfeit drugs. See RAM KAMATH & SCOTT MCKIBBIN, ILL. DEP'T OF CENT. MGMT. SERV., REPORT ON FEASIBILITY OF EMPLOYEES AND RETIREES PURCHASING PRESCRIPTION DRUGS FROM CANADIAN PHARMACIES 11 (2003), available at [http://www.i-saverx.net/assetsrx/canadian\\_rx\\_report.pdf](http://www.i-saverx.net/assetsrx/canadian_rx_report.pdf). That argument is speculative at best, even on the assumption that the scheme will function, on implementation, precisely as designed.

<sup>49</sup> See Thompson, *supra* note 8.

<sup>50</sup> See Pear, *supra* note 8.

<sup>51</sup> See, e.g., Letter from Randall W. Lutter, Acting Associate Commissioner for Policy Planning, Food and Drug Administration, to Honorable Greg Abbott, Attorney General of the State of Texas (Jul. 27, 2005), available at <http://www.fda.gov/oc/opacom/hottopics/importdrugs/abbott072705.html> (contemplated Texas program not permitted); Letter from Randall W. Lutter, Acting Associate Commissioner for Policy and Planning, U.S. Food and Drug Administration, to Douglas M. Duncan, County Executive, Montgomery County Maryland Office of the County Executive (Nov. 8, 2005), available at <http://www.fda.gov/oc/opacom/hottopics/importdrugs/duncan110805.html> (FDA cannot issue waiver for program liable to involve illegal imports);. Copies of these, and additional letters, may be found at <http://www.fda.gov/importeddrugs> (last visited May 9, 2006).

considered such bills in 2005 alone, although most did not enact them; however, at least one State Attorney General has postponed implementation of an enacted statute in response to FDA warnings of illegality.<sup>52</sup>

B. THE ARCHITECTURE OF PRICE DISCRIMINATION ACROSS THE 49<sup>TH</sup> PARALLEL, AND BEYOND<sup>53</sup>

Consumers of any good may be more or less price sensitive, and many U.S. consumers have found drug prices to be high and rising—not surprising, perhaps, as prescription drug spending has risen consistently in recent years, outpacing, among other things, all other categories of healthcare expenditures.<sup>54</sup> In response, many U.S. consumers have become especially price conscious, seeking not just substitute goods (and services), but substitute channels of supply.<sup>55</sup> Moreover, a perception that *identical* goods are subject to radical price disparities across an arbitrary boundary has given rise to a sense of inequity or unfairness, as conspicuous price discrimination may be wont to do more generally.<sup>56</sup> Hence, we note public pressure for the legislation mentioned above, as well as *sub rosa* importation from Canada, Mexico, and, to a lesser extent, the European Union and Asia.<sup>57</sup>

The question of equitable pricing is far from trivial and I do not mean to settle it here. What prices *ought* to be, within or across borders, is a complex matter to be left for other days. Before continuing, I offer merely a few brief comments directed at the supposition that pricing ought to be uniform. First, just as U.S. law recognizes that certain forms of price discrimination play an important role in competitive markets, we ought not to expect uniform pricing across the U.S. market or across international borders.<sup>58</sup> Second, the degree to which we should wish to import

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<sup>52</sup> See, e.g., S.B. 410, §§ 36-43, 79<sup>th</sup> Leg. (Tex. 2005); Susan Konig, *Texas Postpones Drug Importation from Canada*, HEALTH CARE NEWS, Oct. 1, 2005, <http://www.heartland.org/Article.cfm?artId=17760> (implementation postponed by Texas Attorney General Greg Abbott); National Conference of State Legislatures, *supra* note 3 and accompanying text.

<sup>53</sup> The term “49<sup>th</sup> Parallel” is used here in its colloquial sense as descriptive of the US/Canada border, although in fact it describes merely a portion of that border, as Canada’s two most populous cities lie south of the parallel and the largest of the United States lies north of it.

<sup>54</sup> See CONG. BUDGET OFFICE, *supra* note 26, at 1; Heather Won Tesoriero, *Drug Firms Raised Prices 5.5% in First Half of Year*, WALL ST. J., Aug. 2, 2005, at D4 (observing a 5.5% increase in drug prices in the first half of 2005, roughly equivalent to the hike in the first half of 2004); KAISER FAMILY FOUND., *PRESCRIPTION DRUG TRENDS 1* (2004) <http://www.kff.org/rxdrugs/upload/Prescription-Drug-Trends-October-2004-UPDATE.pdf> (double-digit growth each of last eight years).

<sup>55</sup> See Belluck, *supra* note 2 (regarding private sources of re-importation from Canada); Kathleen Doheny, *Think Twice Before Buying Prescription Drugs in Mexico*, L.A. TIMES, Aug. 8, 2004, at L3 (high percentage of counterfeit drugs and legal issues in importation).

<sup>56</sup> See, e.g., *International Prescription Drug Parity: Are Americans Being Protected or Gouged?*, *supra* note 11.

<sup>57</sup> See Belluck, *supra* note 2 (regarding private access to Canadian markets); Connolly, *supra* note 6 (regarding purchases from Canada, Mexico, and Europe); Doheny, *supra* note 55 (regarding purchases from Mexico); Kaufman, *supra* note 2 (regarding public access to Canadian markets). We note too, what will be explained more fully below; that is, that consumer perceptions of identity or similarity between goods may, as perceptions, be more or less accurate in any given case. More generally, both within and across borders, goods may be perceived as close or even perfect substitutes independent of any technical analysis of the goods in question.

<sup>58</sup> For example, prohibited “price discrimination” under the Robinson-Patman Act has been read somewhat narrowly by the courts, with good reason. As a consequence, much of the price differentiation observed in diverse markets has not been held violative of Section 2(a) of the Robinson-Patman Act. See Robinson-Patman Act, 15 U.S.C. 13(a) (2000). For example, the Supreme

foreign pricing is at least an open question. In pharmaceuticals, as elsewhere—but perhaps especially in the realm of pharmaceuticals—we may wish to tolerate a measure of supra-competitive pricing and a corresponding degree of deadweight loss. Perhaps more accurately, deadweight loss today may pay dividends tomorrow, and to the extent we care about both present *and* future welfare, we may very reasonably seek to maximize social welfare diachronically, rather than synchronically.<sup>59</sup> Third, to the extent we wish to permit (and in certain cases award) innovators a substantial degree of market power, we might view price discrimination as a neutral or even beneficial phenomenon. In abstract, price discrimination does not imply cost shifting, is not obviously pernicious, and may serve substantially to reduce whatever deadweight loss is implicated by any given set of IP protections.<sup>60</sup> Finally, Ramsey Optimal Pricing may represent—at least for some—a model of equity in price discrimination across populations.<sup>61</sup>

That less expensive prescription drugs are available in Canadian pharmacies is clear; less clear are the magnitude and distribution of cost differentials across the

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Court has held that prohibited pricing under Robinson-Patman, “is of the same general character as the injury inflicted by predatory pricing schemes actionable under § 2 of the Sherman Act.” *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 221 (1993) (distinguishing anti-competitive below-cost pricing from mere price differentiation or competitive pricing).

<sup>59</sup> Because competitive pricing entails no economic profits, it provides no incentives for the long-term and risky investments required for pharmaceuticals development. We confer patent rights (and other IP protection) because the promise of a degree of monopoly pricing power is incentive to the investment required to develop useful—indeed socially important—goods. Although monopolist pricing may implicate deadweight loss with regard to extant goods, such goods would not be developed in the first place without economically adequate incentives. This is *the* common rationale for patents generally, and one that may be especially applicable to drugs and biologics. *See, e.g.*, Danzon & Towse, *supra* note 20, at 184–85 (patents offset high cost of pharmaceutical R&D); Tomas J. Philipson et. al., *IP & External Consumption Effects: Generalizations from Health Care Markets*, (Nat'l Bureau of Econ. Research, Working Paper No. 11930, 2006) (combining problem of technological change for goods with external consumption effects with problem of generating adequate R&D for goods with private consumption effects). One might suppose that, if there is no general solution to the problem of optimizing IP policy, any set of protections is as good as any other. I think, however, on pragmatic grounds that developed economies would do well to avoid vitiating extant protections.

<sup>60</sup> In brief, once we allocate some degree of market power to a manufacturer (or other seller), that manufacturer will seek to maximize profits by exploiting that market power, as constrained by market demand. In the pure case, any marginal increment in price from the monopolist's profit maximizing price will *decrease* net revenue. This basic principle holds true in each market, whether a manufacturer sells to one market or many. Hence, whatever else we might think of lower prices (via public constraints or otherwise) in markets separate and isolated from our own, we should not imagine that monopolists raise prices at home to “make up” for suppressed revenues abroad. *See* Danzon & Towse, *supra* note 20, at 189–90 (providing a succinct discussion of welfare effects and cost shifting issues).

<sup>61</sup> Ramsey price discrimination (Ramsey Optimal Pricing or Ramsey Pricing) is a straightforward extension of Frank Ramsey's solution to the problem of designing a proportionate tax system so that it can raise a given revenue while imposing a minimum decrease in utility. F.P. Ramsey, *A Contribution to the Theory of Taxation*, 37 THE ECON. J. 47, 47 (1927). Ramsey pricing is formally isomorphic with monopolist price discrimination, but subject to a profit constraint; depending on the level of grain at which it can be implemented, it can, in the limit, serve to eliminate entirely the deadweight loss associated with monopoly pricing. *See, e.g.*, Danzon & Towse, *supra* note 20, at 183 (differential pricing, based on Ramsey pricing principles, is the second best efficient means of paying for the global joint costs of pharmaceutical R&D); JAYASHREE WATAL, WORLD TRADE ORGANIZATION, WORKSHOP ON DIFFERENTIAL PRICING AND FINANCING OF ESSENTIAL DRUGS: BACKGROUND NOTE 11-15 (2001), *available at* [http://www.wto.org/english/tratop\\_e/trips\\_e/wto\\_background\\_e.pdf](http://www.wto.org/english/tratop_e/trips_e/wto_background_e.pdf) (differential pricing allows large fixed research and development costs to be recovered with minimal distortions in resource allocation while allowing provision of lower cost drugs to low income nations; parallel trade can disturb favorable balance of Ramsey Optimal Pricing).

two markets. Retail market comparisons have proven sample dependent and contentious.<sup>62</sup> Describing price differentials is confounded by variation within each of the two markets and, in some instances, by commensurability issues across different dosage, packaging, and distribution systems.<sup>63</sup> Nonetheless, two rough generalities are defensible: First, average retail prices for patent-protected prescription pharmaceuticals are significantly lower in Canada than they are in the U.S.; and second, average retail prices for generic prescription pharmaceuticals are not.<sup>64</sup>

Cross-border price comparisons are in several ways complicated. First, it is not the case that the two markets offer an identical range of products.<sup>65</sup> Apart from packaging and labeling differences, we note that numerous products differ in dosage and modes of delivery across the border and that prescribing habits may likewise differ.<sup>66</sup> Moreover, although the large majority of market-leading, approved molecules in the U.S. market are available in some form in Canada, a significant percentage of new molecule products may be available in one country but not the other—most typically, new products will be available in the U.S. but not in Canada.<sup>67</sup> Patricia Danzon has observed that there is a sort of sampling dilemma in international market comparisons: Price comparisons based on “identical” products inevitably involve relatively small and unrepresentative samples whereas market-wide comparisons inevitably involve a loss of standardization.<sup>68</sup> In addition, even those products available in what we might think of as “identical,” or pharmacologically equivalent form (equivalent formulation, dosage, and delivery) show substantial variation in *relative* prices across the border.<sup>69</sup>

Second, there is significant wholesale price differentiation within the U.S. and, not incidentally, significant variation in price across retail consumers. Federally funded drug purchases have no consistent wholesale price base. The federal government is prohibited, by statute, from imposing formulary requirements or price controls on drug purchases covered under the Medicare program.<sup>70</sup> At the same time, prices paid under other government programs are not similarly constrained. Direct purchases by, e.g., the Department of Veterans Affairs and the Department of Defense, are indexed to lowest-available-wholesale-prices via the Federal Supply

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<sup>62</sup> Compare STAFF OF H. COMM. ON GOVT. REFORM & OVERSIGHT, 105<sup>TH</sup> CONG., PRESCRIPTION DRUG PRICING IN THE 1<sup>ST</sup> CONGRESSIONAL DISTRICT IN MAINE: AN INTERNATIONAL PRICE COMPARISON 4-8 (1998) (comparing Maine retail prices for ten drugs with prices in Canada & Mexico), with DANZON, *supra* note 12, at 2 (concluding that “Minority Staff Reports are based on flawed methodology that leads to seriously upward biased estimates of the price differences between sectors in the US and between the US and Canada and Mexico”).

<sup>63</sup> See Danzon & Furukawa, *supra* note 12, at 522.

<sup>64</sup> See *id.* at 527-28 (reporting Canadian prices for on-patent originator products as 64% of U.S. prices), and at 525-26 (observing slightly lower Canadian prices for generics across data set); *cf.* OFFICE OF PLANNING, U.S. FOOD AND DRUG ADMIN., FDA WHITE PAPER: GENERIC DRUG PRICES IN THE U.S. ARE LOWER THAN DRUG PRICES IN CANADA (2003), available at <http://www.fda.gov/oc/whitepapers/drugprices.html> (most of largest selling chronic use generics less expensive in U.S.).

<sup>65</sup> See Danzon & Furukawa, *supra* note 12, at 522.

<sup>66</sup> See *id.*

<sup>67</sup> See *id.* at 531-32.

<sup>68</sup> See *id.* at 522.

<sup>69</sup> See *id.* at 531-32.

<sup>70</sup> Under the “noninterference” provision of the Act, “the Secretary--(1) may not interfere with the negotiations between drug manufacturers and pharmacies and PDP sponsors; and (2) may not require a particular formulary or institute a price structure for the reimbursement of covered part D drugs.” 42 U.S.C.A. § 1395w-111(i) (West Supp. 2005).

Schedule and General Accounting Office regulations.<sup>71</sup> And although there are no provisions for the exercise of federal buying power with regard to Medicaid covered drugs, the States are permitted to negotiate prices for drugs listed on their Medicaid formularies.<sup>72</sup> Private purchasers may exert substantial market power or none: Large managed care health plans pay, on average, considerably lower prices than do individual, uncovered retail consumers, who pay the highest prices of all.<sup>73</sup> Hospital prices vary, with HMO-owned facilities often paying best wholesale prices and unaffiliated hospitals paying closer to retail.<sup>74</sup> Out-of-pocket expenditures vary substantially across consumers—utilization is, of course, highly variable, and so are the forms of prescription drug coverage to which consumers may have access.<sup>75</sup>

Third, differing market conditions may imply different net costs, which may be reflected in different retail prices in turn. In addition to the different volume packaging, distribution, and delivery differences we have mentioned, are variations in, e.g., exchange rates, income effects, and the liability costs imposed under the U.S. and Canadian legal systems.<sup>76</sup>

Given that the ideal whole markets comparison is thus elusive, it may not be surprising that reported price differences have proven highly sample dependent, variable, and, indeed, controversial.<sup>77</sup> Still, we might venture a few generalizations on the way to asking what cross-border disparities *ought* to be. First, cross-border price differentials are smallest—perhaps negligible, net of distribution and liability costs—with regard to generic products.<sup>78</sup> Indeed, generic prices are lower in the U.S. than in all other countries, except for Canada.<sup>79</sup> That is especially significant, as generics have taken a majority share of the U.S. market, tallied by number of prescriptions, and that share is rising, with generic (ANDA) applications on the increase and a substantial portion of the protected pharmacopoeia going off-patent in the coming decade.<sup>80</sup>

Second, patent-protected pioneer prescription drugs are, *on average*, significantly more expensive in the U.S. than in Canada. Average Canadian wholesale prices are roughly a third lower than average U.S. prices, with significant variation in relative pricing across the market.<sup>81</sup> Because of that difference, the variance, and the disparate forms of prescription drug coverage to which Americans

<sup>71</sup> See 38 U.S.C. §8126 (2000) (Federal Supply Schedule for Department of Defense, Department of Veterans Affairs, Public Health Service, Coast Guard, and Indian Health Service purchases); U.S. DEP'T OF HEALTH & HUMAN SERV., REPORT TO THE PRESIDENT, PRESCRIPTION DRUG COVERAGE, SPENDING, UTILIZATION, AND PRICES 108 (2000), available at <http://aspe.hhs.gov/health/reports/drugstudy> (regarding negotiation of prices).

<sup>72</sup> See *Pharm. Research & Mfrs. of Am. v. Walsh*, 538 U.S. 644, 669-70 (2003) (upholding Maine formulary and pricing scheme).

<sup>73</sup> See, e.g., U.S. DEPT. OF HEALTH & HUMAN SERV., *supra* note 71, at 96, 98 (uninsured consumers may pay 70-100% more than federal and other U.S. purchasers).

<sup>74</sup> See *id.* at 106-107.

<sup>75</sup> See *id.* at 10-20 (regarding different forms of coverage in population).

<sup>76</sup> See generally Richard L. Manning, *Products Liability and Prescription Drug Prices in Canada and the United States*, 40 J.L. & ECON. 203 (1997) (regarding effects of different tort regimes).

<sup>77</sup> See *supra* note 62 (comparing Minority Staff Report and Danzon analyses of price disparities).

<sup>78</sup> See *supra* note 12 (comparing Danzon & Furukawa estimate with FDA White Paper).

<sup>79</sup> See Danzon & Furukawa, *supra* note 12, at 527-528.

<sup>80</sup> See Aaron Smith, *Generic Drug Flood Headed Our Way*, CNNMONEY, Aug. 3, 2005, <http://money.cnn.com/2005/08/03/news/fortune500/generic/index.htm> (branded drugs going off-patent in next five years and spike in generic applications).

<sup>81</sup> See Danzon & Furukawa, *supra* note 12, at 526.

have (and fail to have) access, it ought not to be surprising that retail and out-of-pocket price differences are, for some consumers, and some drugs, extremely high.<sup>82</sup> In that regard, even the most deeply flawed market comparisons may be useful as possible case studies—they highlight the fact that, for some retail market baskets of prescription drugs, cross-border price disparities can be marked, at double or more the average differential.<sup>83</sup>

Third, the rough architecture of price differentials is approximately what we would expect. Generic products are comparably priced because the prescription generic markets—especially the unbranded prescription generic markets—are approximately competitive, leaving relatively little room for price discrimination on either side of the border.<sup>84</sup> Substantial gaps are found with on-patent pioneer products because profit-maximizing manufacturers can exert a greater degree of market power for this class of drugs.<sup>85</sup> Within this class, relative prices will vary because both the degree of manufacturer market power and the consumers' price elasticity of demand are neither fixed nor constant by dint of patent protection. The ordinal of the price differentials corresponds to the relative affluence of the national markets, construed as national markets.

Still, although the price gap shrinks considerably when adjusted for income differences, we do not, as a general matter, observe Ramsey Optimal price differentials across the border.<sup>86</sup> The gap between predicted Ramsey differentials is greater still with regard to several European nations.<sup>87</sup> Neither observation should be surprising, as Canada and EU member states subject pharmaceuticals to various regulatory price constraints or pressures; hence, observed price differentials are not merely the product of monopolist response to national wealth differences.<sup>88</sup> To the

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<sup>82</sup> See STAFF OF H. COMM. ON GOVERNMENT. REFORM & OVERSIGHT, *supra* note 62, at 11-15; Press Release, Public Citizen, State Drug Price Surveys Find Seniors Pay Double (Nov. 8, 1999), <http://www.citizen.org/pressroom/release.cfm?ID=427>.

<sup>83</sup> See, e.g., Press Release, Public Citizen, *supra* note 82 (reporting double and near-double retail prices). DANZON, *supra* note 12, has sharp and sound criticism for the methodology employed in STAFF OF H. COMM. ON GOVERNMENT. REFORM & OVERSIGHT, *supra* note 62. That criticism does not impugn however, the underlying observations of extreme price disparities for some retail drug purchases.

<sup>84</sup> Although there is some disagreement as to the particulars, depending on sample sets, generic prices appear roughly competitive on both sides of the border. Compare Danzon & Furukawa, *supra* note 12, at 525-526 (observing slightly lower Canadian prices for generics across data set); with OFFICE OF PLANNING, *supra* note 64.

<sup>85</sup> See Danzon & Furukawa, *supra* note 12, at 526.

<sup>86</sup> That is, differential are not completely explained by differences in wealth and costs. See Danzon & Furukawa, *supra* note 12, at 527-530. Neither do we observe Ramsey discrimination within our borders, as demand is partitioned not just according to ability/willingness to pay, but according to regulation and varying degrees of market power to which consumers may be assigned by, among other things, public and private accident. For a brief summary of the notion of Ramsey price discrimination, see *supra* note 61.

<sup>87</sup> See *supra* note 61.

<sup>88</sup> Within the EU, price discrimination is further complicated by provisions for parallel trade amongst member states. See, e.g., Catriona Hatton and Wim Nauwelaerts, *Parallel Justice?*, *Pharma Times* 54-55 (Mar. 2004) (regarding policy issues behind Bayer-Adelat case) at [www.pharmatimes.com](http://www.pharmatimes.com). Although manufacturers may exert downstream control via, e.g., contractual provisions, the trade suspension of the regulatory borders between member states renders the partitions requisite for price discrimination all the more porous. Moreover, the extent to which the EU will permit such downstream controls remains unsettled. See Catriona Hatton and Wim Nauwelaerts, *European Court Opens a Small Window of Opportunity for Pharmaceutical Companies to Restrict Parallel Imports of Medicines*, *European Pharmaceutical Contractor* 30-31 (Aug. 1, 2004), available at <http://www.hllaw.com/files/Publication/937ed0df-08d0-4722-9cae->

extent we consider Ramsey pricing a normative baseline for appropriate cross-border price differentials, this is, at least, *prima facie* ground for questioning the IP-price-trade-regulation structure that allows the differentials we do observe, both as they bear on U.S. pricing and as they may raise questions of foreign free-riding on U.S. research and development expenditures.

### III. ERASING THE DOTTED LINE: WHAT WILL (LIKELY) HAPPEN TO PRICE AND SUPPLY IF IMPEDIMENTS TO TRADE ARE LIFTED?

The prohibition in federal law notwithstanding, the importation—or smuggling—of prescription drugs is ongoing. Private citizens have had access to Canadian pharmacies on an *ad hoc* basis, and additional importation has taken place in response to various State initiatives.<sup>89</sup> Although enrollment in many State sponsored plans has been considerably smaller than projected by the States themselves, it has been substantial nonetheless.<sup>90</sup> We should distinguish, however, two questions. First, is the question whether some U.S. citizens may, in the short run, take advantage of cross-border price disparities. Second, is the question whether lifting a ban on re-importation from Canada holds promise as a means of substantially reducing U.S. drug expenditures. That we may answer the first question in the affirmative says relatively little about how we should answer the second.<sup>91</sup>

With regard to the second question, I suggest that it is implausible to think that access to the Canadian market holds much promise, in part because Canada's market is considerably smaller than the U.S. market and in part because lifting the regulatory barrier to parallel trade is inadequate to guarantee free access to that market, small or not.<sup>92</sup> To suppose otherwise is to suppose (a) that U.S. manufacturers will take no lawful steps to protect their revenue streams; (b) that the Canadian government will take no lawful steps to protect its access to pharmaceuticals; and (c) that Canadian citizens will not themselves compete on price on the remainder. Each of these suppositions is implausible on its face.

U.S. manufacturers have various lawful means at their disposal should they wish to block—or manage—parallel trade in pharmaceuticals. Note, first, that there is no reason to expect that U.S. firms (and international firms in the U.S. market) will undercut their own market positions by tailoring their exports to suit cross-border arbitrage.<sup>93</sup> Present export levels thus constitute a theoretical upper bound on

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<sup>89</sup> See, e.g., S.B. 410, §§ 36-43 (Tex. 2005); Belluck, *supra* note 2 (regarding private *sub rosa* importation); Kaufman, *supra* note 2 (regarding a State government engineered importation scheme); National Conference of State Legislatures, *supra* note 3 (regarding National Conference of State Legislatures summary).

<sup>90</sup> See *Illinois Seeking More Prescription Imports*, VT. GUARDIAN, Aug. 5, 2005, at x, available at [http://www.i-saverx.net/assetsrx/080505\\_vermont.pdf](http://www.i-saverx.net/assetsrx/080505_vermont.pdf). (fewer than 15,000 consumers registered across five states); *Just How Does Governor Define Success in State's Program to Import Prescription Drugs?*, HERALD & REVIEW (Decatur), Oct. 18, 2005, at x, available at <http://www.herald-review.com/articles/2005/10/19/news/editorials/1010687.txt> (roughly 14,000 prescriptions filled for roughly 27 million eligible persons in five states).

<sup>91</sup> And, as remarked above, brackets the question whether we should wish to import foreign pricing schemes. See *supra* text accompanying notes 59-61.

<sup>92</sup> For a brief catalogue of the limitations of parallel trade, as a means of price control, see CONG. BUDGET OFFICE, *supra* note 26, at 4-5.

<sup>93</sup> See *id.* at 5 (regarding various manufacturer responses); Ceci Connolly, *Pfizer Cuts Supplies to Canadian Drugstores; Sales are Halted to Reimporters of Bargain Drugs*, WASH. POST,

potential re-importation, and an implausibly high one at that. Independent of contractual obligations to particular Canadian buyers, U.S. firms are under no special obligation to maintain exports to Canada at current levels.<sup>94</sup> U.S. firms may also, by contract, establish downstream controls on distribution in excess of those currently employed.<sup>95</sup> In fact, such strategies may be applied wholesale or piecemeal; and it appears that each has been employed to some extent to manage arbitrage under the present legal regime.<sup>96</sup>

Second, Canada has various lawful means at its disposal for blocking—or managing—arbitrage that undercuts the supply of pharmaceuticals in Canadian markets. Public and private buyers in Canada may negotiate their own contractual protections, especially as such protections may be advantageous to both upstream and downstream parties in the chain of distribution. In addition, just as Canada benefits from impediments to parallel trade established, at the border, in U.S. law, so Canada may seek to establish its own statutory impediments to exportation. In fact, the Canadian Parliament has been contemplating legislation to do precisely that, blocking the bulk exportation of U.S.-manufactured pharmaceuticals back into the U.S.<sup>97</sup> Such legislation does not obviously run afoul of anti-dumping or countervailing duties obligations, as it confers no special advantage on Canadian manufacturers nor any special burden on the U.S. manufacturers whose production is at issue.<sup>98</sup>

Perhaps it is not surprising, then, that bulk re-importers have already begun to look further afield for their supply of low-cost pharmaceuticals. I-SaveRx, the Illinois sponsored re-importation to which several states have sought access, has already begun to look to Australian and New Zealand drug distributors to meet the demand for low cost pharmaceuticals, despite the nascent state of re-importation and the fact that participation has lagged behind early projections by a considerable margin.<sup>99</sup> Indeed, I-SaveRx appears to be seeking still wider channels of supply, as

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Feb. 19, 2004, at A10 (preliminary cutbacks by one major pharmaceutical manufacturer); *Merck Shuts Off Canadian Pharmacies Selling to U.S.*, BLOOMBERG NEWS, Jan. 19, 2005, <http://www.bloomberg.com/apps/news?pid=1000082&sid=ai9RdezyHWRE&refer=canada> (regarding cutbacks by Merck, Pfizer Inc., AstraZeneca Plc, and Wyeth).

<sup>94</sup> See Connolly, *supra* note 93; *Merck Shuts Off Canadian Pharmacies Selling to U.S.*, *supra* note 93.

<sup>95</sup> See CONG. BUDGET OFFICE, *supra* note 26, at 5.

<sup>96</sup> See *supra* notes 90-91.

<sup>97</sup> See, e.g., Reuters, *supra* note 9 (regarding legislative controls being suggested by Canada's Health Minister).

<sup>98</sup> See World Trade Org., Agreement on the Implementation of Article VI of the General Agreement on Tariffs and Trade 1994, [http://www.wto.org/english/docs\\_e/legal\\_e/19-adp.pdf](http://www.wto.org/english/docs_e/legal_e/19-adp.pdf) (regarding anti-dumping provisions); World Trade Org., Agreement on Subsidies and Countervailing Measures, [http://www.wto.org/english/docs\\_e/legal\\_e/24-scm.pdf](http://www.wto.org/english/docs_e/legal_e/24-scm.pdf).

<sup>99</sup> As of October 2005, the I-SaveRx web site reports sourcing in Canada, Ireland, and the U.K., while reporting separate Illinois feasibility studies regarding Canada, Australia/New Zealand, and the E.U. See Welcome to I-SaveRx, <http://www.i-saverx.net/> (last visited May 9, 2005). Illinois has announced that it intends to add Australia and New Zealand sourced drugs to the I-SaveRx program. See Press Release, The Democratic Party of Wisconsin, Governor Doyle, Illinois Governor Blagojevich, and Illinois Congressman Emmanuel Announce Expansion of I-SaveRx Prescription Drug Program (July 18, 2005), available at [http://www.i-saverx.net/assetsrx/071905\\_dpw.pdf](http://www.i-saverx.net/assetsrx/071905_dpw.pdf) (report issued by Democratic Party of Wisconsin). Such broad sourcing has been sought despite the fact that, across five states, only about 14,000 consumers have even registered for the program. See *Illinois Seeking More Prescription Imports*, *supra* note 90.

at least one of its major sources of imports, CanaRx, has raised the topic of Indian sourcing of pharmaceuticals.<sup>100</sup>

Finally, should Canadian supply dwindle significantly, we might expect a non-trivial number of Canadians to compete with re-importers on price. Despite considerable public support for medical services in Canada, there is, already, substantial access to other segments of the U.S. healthcare market by Canadian citizens, the majority of whom live a relatively short distance from the U.S. border. It is an empirical question whether true open-market prices across the U.S./Canada border would be significantly lower if that market could somehow be accomplished; and despite lower per-capita GDP in Canada,<sup>101</sup> it is not analytically false that they might be slightly higher.

Hence, we ought not to be surprised that the Congressional Budget Office has predicted that full-scale, lawful re-importation would make only a “negligible” impact on U.S. prescription drug prices.<sup>102</sup> That is, a negligible impact independent of its regulatory burden. I shall argue below that the burden is more substantial than it might appear.

#### IV. OPEN BORDERS AND THE COST OF FREE TRADE

The main argument of this paper comes in two parts. I have argued that Canadian re-importation is inadequate as a means of controlling the price of prescription drugs in the U.S. That is partly to do with the fact that Canada has a much smaller pharmaceuticals market than we do and partly to do with the fact that re-importation is, *qua* price regulation, baroque and fragile.<sup>103</sup> Second, I shall argue that the benefits of parallel trade in pharmaceuticals—such as they may be—are not to be had for free. There are real regulatory burdens implied by parallel trade, burdens that do not carry their own weight if the benefits are likely slight and transitory. Central to this second argument is the notion that the pharmaceuticals market *wants* regulation; that is, the pharmaceuticals market has all the earmarks of classic, Coasian market failure and, as such, ought to be subject to the sort of comprehensive regulatory scheme to which it is, in fact, subject.<sup>104</sup>

That the market is subject to such regulation on both sides of the border raises, but does not answer, the question what sorts of regulatory similarity are adequate to what purposes. If our purpose is to maintain regulatory integrity as products travel in international commerce, we must ask about the particular regulatory burdens imposed by trade *across* borders, as adequate local regimes may not be mutually transparent and as there may be a sort of regulatory gap between jurisdictions, despite adequate compliance within them.<sup>105</sup> Importation and exportation may thus

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<sup>100</sup> *FDA Seizes Drugs Imported Under States' Program, Supplier Says*, BLOOMBERG NEWS, Mar. 9, 2005, <http://www.bloomberg.com/apps/news?pid=10000082&sid=atBleFFijT6E&refer=canada#>.

<sup>101</sup> For a summary comparison of economic indicators, including relative wealth, see ORGANISATION FOR ECONOMIC CO-OPERATION & DEVELOPMENT, OECD IN FIGURES 12-13 (Supp. 2005), available at <http://213.253.134.29/oecd/pdfs/browseit/0105061E.PDF>.

<sup>102</sup> CONG. BUDGET OFFICE, *supra* note 26, at 5.

<sup>103</sup> As above, this observation holds independent of the extent to which such controls may be otherwise undesirable.

<sup>104</sup> See generally Coase, *supra* note 25 (regarding social costs amenable to administrative management).

<sup>105</sup> The gap may be observed at various levels of regulation and compliance. For example, just as the administrative burdens of regulating foreign distributors may seem daunting to FDA, especially as we consider greatly expanding the pool of such distributors, so may the burdens of regulating

involve costs above and beyond those of transportation itself. We need to know what those costs are and who is likely to bear them. Finally, we may be concerned about ersatz parallel trade; that is, we may wonder about the extent to which we foster or subsidize less desirable substitute trade channels when we multiply lawful ones.

#### A. THE ARGUMENT FOR REGULATION, IN BRIEF

I am unaware of popular arguments against the regulation of pharmaceuticals and, in particular, biotech products. It is true that arguments against regulation generally have had *some* purchase.<sup>106</sup> Still, such broad arguments do not come from dominant views of administrative governance. More to the point, there seems not to have been much serious discussion in the U.S., Canada, or the E.U., of the notion that drug products are especially bad candidates for safety regulation or especially good candidates for purely private controls, or perhaps purely private controls augmented by the tort system.<sup>107</sup> To the contrary, if we bracket advocacy of parallel trade, popular and academic concerns about pharmaceuticals regulation appear most commonly directed at inadequate consumer protection, not excessive regulation.<sup>108</sup>

Re-importation advocacy, however, typically involves some sort of notion that a particular regulatory regime might be just as well suspended. Hence, consumers (a) ought to be able to choose amongst competing regulatory regimes as they might choose amongst competing *brands*, (b) ought to be able to choose amongst “equivalent” regulatory regimes, or (c) ought to be able to opt out of regulation, at least for certain purposes. If our central concern about drugs is *price*, we might well seek substitute channels of supply, just as we might seek substitute products. Alternative regulatory regimes *can* be construed as describing yet another vector along which consumers may differentiate competing products. With or without incorporating that vector, the market may perceive competing products as more-or-less close substitutes. Perhaps, however, we ought to be chary of suggestions that we suspend regulatory efforts in this particular case and careful, *at least*, in how we frame the issue of regulatory substitution.

In his seminal work on “those actions of business firms which have harmful effects on others,” R.H. Coase considered generally the circumstances under which third-party effects may best be handled by market transactions on the one hand or

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exportation be seen as daunting by the Canadian government if they are to regard retail outlets at various scales as potential exporters. In fact, Health Canada has declined to assure the integrity of such expanded exports as a matter of its own enforcement discretion—it wishes to distribute its limited compliance resources otherwise. *See, e.g.*, citing Health Canada, Letter from Diane C. Gorman, Assistant Deputy Minister, to Richard H. Carmona, Surgeon General of the U.S. Public Health Service (Jun. 1, 2004) available at [http://www.fda.gov/ohrms/dockets/dockets/04n0115/04N-0115\\_emc-000018-01.pdf](http://www.fda.gov/ohrms/dockets/dockets/04n0115/04N-0115_emc-000018-01.pdf).

<sup>106</sup> Less ambitiously, anyone might sensibly question the efficiency of particular regulatory endeavors. Coase himself was acutely aware of the possibility of regulatory inefficiency or failure. *See generally* Coase, *supra* note 25.

<sup>107</sup> *See* Elias Mossialos et al., World Health Organization, *Regulating Pharmaceuticals in Europe: An Overview*, in *REGULATING PHARMACEUTICALS IN EUROPE: STRIVING FOR EFFICIENCY, EQUITY, AND QUALITY 2* (Elias Mossialos et al. eds. 2004) (“The pharmaceutical market is unique with regard to the extent and depth of its failure to meet the criteria for a perfect market.”). Arguments on behalf of common law controls most typically advocate the importance of state tort law as an adjunct to federal regulation, not as its replacement. *See, e.g.*, *Feldman v. Lederle Laboratories*, 625 A.2d 1066, 1079 (N.J. 1993).

<sup>108</sup> Qualify with, e.g., patient advocacy groups concerned with access.

various administrative arrangements on the other.<sup>109</sup> When the cost of the harm is clear and the pricing system works smoothly (that is, strictly speaking, when transaction costs are zero), the optimal allocation of resources will occur via market transaction independent of the initial assignment of rights.<sup>110</sup> When, however, the costs of transacting around the harms are significant, an administrative solution may be most efficient.<sup>111</sup> The administrative solution is most likely to be efficient in circumstances in which the costs of contracting are especially high.<sup>112</sup> Those are, for example, where material contingencies are especially numerous and diverse and where especially long-term contracts are required to address potential harms.<sup>113</sup> Administrative functions may often, of course, be implemented within a firm, but where we seek to administrate over highly complex or diverse effects that are liable to be felt by very large numbers of persons, regulation *within* a firm may be intractable and government regulation may be preferable.<sup>114</sup> Indeed, we might add that, just as long term effects might militate in favor of administrative solutions generally, so especially long term effects might militate in favor of *government* regulation in particular, as intra-firm (and capital markets) discount rates may often be higher than public ones.<sup>115</sup>

Coase provides an example of environmental pollution as suggesting administrative solution via government intervention: “In the standard case of a smoke nuisance, which may affect a vast number of people engaged in a wide variety of activities, the administrative costs might well be so high as to make any attempt to deal with the problem within the confines of a single firm impossible.”<sup>116</sup> Indeed, the possible harms of pharmaceuticals and the contingencies under which they may arise provide an equally good example, if not a better one.<sup>117</sup> Of course

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<sup>109</sup> See Coase, *supra* note 25. Coase provides a useful, general approach that is applicable to our market or domain; other rationales for regulatory intervention are consistent with it, certainly so with regard to our application. E.g. RICHARD POSNER, *ECONOMIC ANALYSIS OF LAW*, 383-385 (6th ed. 2003) (regarding “optimal regulation”).

<sup>110</sup> See Coase, *supra* note 25, at 15. That does not, of course, mean that there are no distributional consequences to the choice of initial allocation or that such consequences—and threshold effects—are not legitimate areas of social concern. Steven Cheung has defined “transaction costs” broadly, as “all those costs that cannot be conceived to exist in a Robinson Crusoe (one-man) economy.” Steven N.S. Cheung, *On the New Institutional Economics*, in *CONTRACT ECONOMICS* 48, 51 (Lars Werin & Hans Wijkander eds., 1992).

<sup>111</sup> See Coase, *supra* note 25, at 16.

<sup>112</sup> *Id.* at 16-17.

<sup>113</sup> *Id.*

<sup>114</sup> See *id.* at 17. Significant attention has been paid to the notion that problems of administration at the level of the firm may be observed in government administration too; Coase himself referred to the government as a “super firm.” Cheung, *supra* note 110, at 57.

<sup>115</sup> See Coase, *supra* note 25, at 17. *C.f.* POSNER, *supra* note 109, at 385 (regarding regulatory intervention for causes of fatal injuries); OFFICE OF MGMT. & BUDGET, EXECUTIVE OFFICE OF THE PRESIDENT, *ECONOMIC ANALYSIS OF FEDERAL REGULATIONS UNDER EXECUTIVE ORDER 12866* (Jan. 11, 1996), <http://www.whitehouse.gov/omb/inforeg/riaguide.html> (regarding intervention in cases of market failure, such as involving externalities, natural monopoly, market power, and inadequate or asymmetric information).

<sup>116</sup> Coase, *supra* note 25, at 17. None of this should be taken to suggest that Coase was insensitive to the costs of government regulation or the possibility of its failure to provide an efficient result. *C.f.* OFFICE OF MGMT. & BUDGET, *supra* note 116 (regarding alternatives to federal regulation).

<sup>117</sup> See, e.g., Mossialos et al., *supra* note 107, at 2 (“The pharmaceutical market is unique with regard to the extent and depth of its failure to meet the criteria for a perfect market.”); WORLD HEALTH ORG., *THE WORLD MEDICINES SITUATION* 75 (2004) (“Worldwide, it is estimated that half of all medicines are inappropriately prescribed, dispensed, or sold, and that half of all patients fail to take their medicines properly.”).

pharmaceuticals are therapeutically useful—often critically so—but their benefits do not come risk-free.<sup>118</sup> It is easy enough to point to *ad hoc* examples of the dangers medications may present. In the limit, drug products may be fatal to their consumers, and such fatal adverse events are a significant cause of death.<sup>119</sup> Short of that, drugs may cause serious trauma, e.g., in the form of cardiac arrest, internal bleeding, organ damage, or serious teratogenic effects if consumed by pregnant women; and such effects may be distributed variously across large populations and time.<sup>120</sup>

FDA has expressed concern that parallel trade might facilitate trade in (and consumption of) counterfeit and otherwise substandard pharmaceuticals and has discovered numerous examples of such products among re-imports, both real and fake.<sup>121</sup> Such products may be dangerous insofar as they are toxic or susceptible to unanticipated drug interactions; and, plainly, they may also do harm if they deprive a patient of an anticipated and otherwise deliverable therapeutic benefit. Such concerns are not parochial to FDA or to the U.S.—the WHO, for example, considers trade in counterfeit drugs to be a burgeoning problem as, apparently, does the EU.<sup>122</sup>

Setting aside concerns that parallel trade may decrease the integrity of the U.S. drug supply does not eliminate the problem, because therapeutic drugs in general—approved, conforming therapeutic drugs that are properly prescribed and administered—are inherently risky and potentially dangerous.<sup>123</sup> Hence we observe, for example, standard regulated labeling regarding “contraindications,” “warnings,” “precautions,” and “adverse events,” for approved drug products.<sup>124</sup> Such labeling devices represent, among other things, risk management tools.<sup>125</sup> In their particulars,

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<sup>118</sup> See generally CTR. FOR DRUG EVALUATION & RESEARCH, U.S. DEPT. OF HEALTH & HUMAN SERVICES, 2001 REPORT TO THE NATION 25-28 (2002), available at <http://www.fda.gov/cder/reports/rtn/2001/rtn2001-3.htm>.

<sup>119</sup> See *id.*

<sup>120</sup> A given drug product may present diverse risks. For example, FDA’s Patient Information Sheet for Isotretinoin (a drug product indicated for the treatment of severe acne) warns against any use during pregnancy, as risks include birth defects, miscarriage, premature birth, and infant death; risks for the population more generally include, but are not limited to, serious mental health problems, serious brain problems, damage to internal organs, and death. U.S. FOOD & DRUG ADMINISTRATION, PATIENT INFORMATION SHEET: ISOTRETINOIN (MARKETED AS ACCUTANE) (Nov. 2005), available at <http://www.fda.gov/cder/drug/InfoSheets/patient/isotretinoinPIS.pdf>.

<sup>121</sup> See, e.g., Press Release, U.S. Food & Drug Administration, Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments (Jan. 27, 2004) (regarding variously nonconforming drugs seized at import mail facilities and courier hubs).

<sup>122</sup> See, e.g., U.K. DEPT. OF HEALTH, EU HEADS OF MEDICINES AGENCIES (HUMAN & VETERINARY) MEETING (2005), available at [http://www.dh.gov.uk/PolicyAndGuidance/International/EuropeanUnion/EUPresidency2005/EUPresidencyArticle/fs/en?CONTENT\\_ID=4117909&chk=aSYUR8](http://www.dh.gov.uk/PolicyAndGuidance/International/EuropeanUnion/EUPresidency2005/EUPresidencyArticle/fs/en?CONTENT_ID=4117909&chk=aSYUR8); WORLD HEALTH ORG., FACT SHEET NO. 275, COUNTERFEIT MEDICINES (Feb. 2006), available at <http://www.who.int/mediacentre/factsheets/fs275/en/print.html>; Reuters, *Fake Drugs Spreading Rapidly, Warns WHO*, MSNBC, May 6, 2005, available at <http://www.msnbc.msn.com/id/776125> (focusing on counterfeit drugs in Asia and developing countries).

<sup>123</sup> See generally CTR. FOR DRUG EVALUATION & RESEARCH, *supra* note 119.

<sup>124</sup> See 21 C.F.R. § 201.57(d)-(g) (2005) (regulations regarding “contraindications,” “warnings,” “precautions,” and “adverse events,” respectively); 21 C.F.R. § 201.57(f)(6) (2005) (regarding categories of teratogenic precautions).

<sup>125</sup> See, e.g., CTR. FOR BIOLOGICS EVALUATION & RESEARCH, U.S. DEPT. OF HEALTH & HUMAN SERVICES, GUIDANCE FOR INDUSTRY: DEVELOPMENT AND USE OF RISK MINIMIZATION ACTION PLANS (2005), available at <http://www.fda.gov/cder/guidance/6358fml.pdf> (regarding appropriate and updated labeling, among other action plans and including labels, practitioner letters, and patient medication guides among RiskMAP tools).

they, like product approvals, are part of what establish any given product as more-or-less safe or effective, for certain indications, in a given population.<sup>126</sup> In their particulars, they may vary across regulatory regimes in ways that matter to the public health, even if both (or all) the regimes in question are, generally speaking, defensible as adequate. In addition, post-marketing scrutiny of drug safety is common across mature regulatory regimes—we impose information gathering, record-keeping, and reporting requirements on all prescription drugs because even substantial and prolonged clinical testing cannot be presumed definitive indicators of a drug's risks.<sup>127</sup> In the U.S., all pharmaceutical and biological manufacturers are subject to adverse event reporting regulations, which require the reporting of adverse events generally and the prompt reporting of certain serious adverse events.<sup>128</sup> For some products, systematic post-approval (Phase 4) testing may also be required.<sup>129</sup> Canada, the EU, and the ICH have developed analogous standards for much the same reasons.<sup>130</sup>

Competition itself can serve as a risk management tool, but perfect competition is elusive—in relevant regards, perhaps especially so in an industry such as this. Perfect competition requires: (a) indefinitely many buyers and sellers, each of which takes price and cost as a given;<sup>131</sup> (b) a consistent, or homogeneous, product across producers;<sup>132</sup> (c) perfect information on the parts of buyers and sellers;<sup>133</sup> (d) free entry;<sup>134</sup> and (e) no third-party effects—or externalities—generated by either the production or acquisition of goods.<sup>135</sup> All of these criteria fail to obtain in pharmaceuticals markets. For any given category of product, sellers may be few or one.<sup>136</sup> Some degree of product differentiation may be the norm—certainly so in

<sup>126</sup> See *supra* text accompanying notes 103-108.

<sup>127</sup> See CTR. FOR DRUG EVALUATION & RESEARCH, *supra* note 119, at 25 (“The practical size of premarketing clinical trials means that we cannot learn everything about the safety of a drug before we approve it. Therefore, a degree of uncertainty always exists about the risks of drugs.”)

<sup>128</sup> See 21 C.F.R. § 314.80 (2005) and 21 C.F.R. § 600.80 (2005) (regulations regarding post-marketing reporting of adverse events for drugs and biological products, respectively); adverse events that are both “serious and unexpected” are subject to 15-day “Alert reports” requirements under 21 C.F.R. § 314.80(c)(1)(i) (2005) and follow-up reporting requirements under 21 C.F.R. § 314.80(c)(1)(ii) (2005). Biologics manufacturers are subject to analogous requirements for “Alert reports” and follow-ups under 21 C.F.R. § 600.80(c)(1)(i)-(ii) (2005); Expedited Safety Reporting Requirements for Human Drug and Biological Products, 62 Fed. Reg. 52237 (Oct. 7, 1997) (to be codified at 21 C.F.R. pt. 20, 310, 312, 314, and 600).

<sup>129</sup> See 21 C.F.R. § 312.85 (2005) (regarding post-marketing “phase 4” studies).

<sup>130</sup> In Europe, pharmacovigilance is required of marketing authorization holders and the competent authorities of the member states under Council Regulation 2309/93, art. 19-26, 1993 O.J. (L 214) (EC); Council Directive 2001/83, 2001 O.J. (L 311) (EC), available at <http://www.eudravigilance.org/human/docs/Directives/Consolidated2001-83EN.pdf>; and Commission Regulation 540/95, 1995 O.J. (L 55) (EC), available at <http://www.eudravigilance.org/human/docs/reg95-540en.pdf>. The EMEA implemented “EudraVigilance,” an adverse event database, in 2001. Information on, and links to, the system, may be found at <http://www.eudravigilance.org/human/index.asp>; Health Canada monitors adverse events for pharmaceutical and biological products, among others through its Canadian Adverse Drug Reaction Monitoring Program (CADRMP). Information regarding the system, and links to the database, may be found at [http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/agreement\\_accord\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/agreement_accord_e.html).

<sup>131</sup> See JACK HIRSCHLEIFER, PRICE THEORY & APPLICATION 198 (1976); KEITH N. HYLTON, ANTITRUST LAW: ECONOMIC THEORY AND COMMON LAW EVOLUTION 4 (2003).

<sup>132</sup> See HYLTON, *supra* note 132, at 8.

<sup>133</sup> See *id.* at 5.

<sup>134</sup> See *id.* at 6.

<sup>135</sup> See *id.* at 7-8.

<sup>136</sup> See 21 C.F.R. §316 (2004). Indeed the Orphan Drug Act contemplates that certain useful drugs are liable not to be developed at all under competitive conditions and the general regulatory

patent-protected products but also across a broad selection of non-exclusive or generic ones.<sup>137</sup> Barriers to entry, including regulatory barriers, are substantial in both the U.S. and Canada.<sup>138</sup> Information is inevitably incomplete and may be staggeringly so, while information asymmetries ranging across buyers and sellers are liable to be spectacular. Drug quality is not generally subject to easy inspection by consumers, and both anticipated benefits and possible harms may be expressed clearly, subtly, or stochastically, and may be evident—if at all—in the short, intermediate, or long run. Third-party effects may be substantial—trivially so with regard to the public health effects of untreated or mistreated infectious diseases and the teratogenic or heritable effects of certain therapies or the conditions those therapies might treat. All of these possibilities militate *against* easy and inexpensive contract formation and *in favor* of administrative solutions.

None of this is news. Public understanding of the range of possible risks and benefits may be variable or often incorrect, in pharmaceuticals as elsewhere. Still, possible side-effects are conspicuous in direct-to-consumer advertising, and labeling aimed at patients and prescribing physicians, and certain adverse events have received considerable public attention. Within regulatory circles, both general notions of drug risks and the particular mechanisms used to detect, evaluate, and report them have received much attention. The point of reviewing these issues here is simply to highlight the extent to which a presumption of regulatory needs ought to permeate any discussion of parallel trade. That such needs have gotten such short shrift in the discussion is at least surprising.

Of course one might be concerned about the costs of regulation as well, but there are reasons to think that the domain of pharmaceuticals is as well suited to regulation as a large market can be. FDA's statutory authority regards risky products, risks which are extremely variable across a very large portion of the population. That authority involves a highly technical subject matter subject to inevitable uncertainties. FDA's centers and offices face clear technical and disciplinary demands—demands which, I suggest, are at least roughly satisfied by FDA's architecture and staff.<sup>139</sup> That is, there is a proper technical subject matter about which the administrative agency may acquire substantial expertise and the

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scheme imposed on drug development. See Pub. L. 97-414 (Jan. 4, 1983) (Congressional Findings for the Orphan Drug Act). The Act's implementing regulations require the drug's sponsor to demonstrate, e.g., that "there is no reasonable expectation" that drug sales will offset development costs or that the target market for the drug is less than 200,000 persons. See 21 C.F.R. §316.21 (2006).

<sup>137</sup> Louis Philips, among others, makes this point about products more generally. See LOUIS PHILIPS, *THE ECONOMICS OF PRICE DISCRIMINATION* 1 (1983) (typical firms have some degree of market power). For a pharmaceutical example, we might consider that, although patent protection continues for certain formulations of Prozac (e.g., Patent Number 5910319, Capsule, Delayed Release Pellets), exclusivity regarding the active moiety itself, as indicated for the treatment of depression, has expired. Numerous generic manufacturers have thus entered the market for this popular drug. At the time of this writing, FDA's listing of Approved Drug Products with Therapeutic Equivalence Evaluations (Electronic Orange Book), current through June 2005, lists more than 22 manufacturers of more than 60 formulations of fluoxetine hydrochloride. U.S. Food & Drug Administration, Electronic Orange Book (2005), <http://www.fda.gov/cder/ob/default.htm>.

<sup>138</sup> The requirements of marketing approval alone are among the most stringent in all of administrative law. See, e.g., 21 C.F.R. § 314 (2005) (U.S. regulations regarding applications to FDA for approval to market a new drug); Food and Drug Regulations (Food and Drugs Act), C.R.C. C.08.002 (regulations regarding sale or advertising of new drugs in Canada).

<sup>139</sup> Lars Noah, *Rewarding Regulatory Compliance: the Pursuit of Symmetry in Products Liability*, 88 GEO. L.J. 2147, 2153-57 (2000) (regarding agency as expert authority).

agency has, in fact, acquired such expertise.<sup>140</sup> No private firm, nor any of the several States, has done anything comparable.

Thus, we have a brief argument for the typically non-controversial position that serious regulation—a comprehensive regulatory scheme—is critical to the proper functioning of markets in pharmaceuticals and, not incidentally, public health. Introducing additional types of systematic error into consumer decision-making, or exacerbating existing ones, might subject millions or tens of millions of persons to harm. The general question whether free trade in pharmaceuticals is liable to enhance or confound the relevant *regulatory* task is not, from the U.S. perspective, substantially more difficult. The large majority of the world's nations lack any effective pharmaceuticals regulation and if drug counterfeiting is a problem globally, it is a special problem in Asia, where at least two nations possess both problematic IP regimes and significant manufacturing capacity;<sup>141</sup> correspondingly, they have been identified as active producers and substantial exporters of counterfeit drug products.<sup>142</sup> Any under-regulated nation might be a source of counterfeit or otherwise substandard medicines; certainly, many have been.<sup>143</sup>

Parallel trade amongst nations that possess substantial regulatory regimes poses a smaller, but overlapping, set of problems. The stock of approved products may vary across borders—as it varies across the U.S./Canada border—and similar products may present differences in labeling, packaging, or dosage that have regulatory (and safety) significance on either side of the border. Enforcement provisions or priorities may vary across borders, too, in ways relevant to a nation's applied risk/benefit analysis.<sup>144</sup> And additional channels of *bona fide* trade may foster additional opportunities for mistake or fraud. For example, State-endorsed importation web sites may themselves be sources of non-complying products—say, due to flaws in the chain of distribution or mistakes about purported product

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<sup>140</sup> See *id.* Of course, this is not to say that the Agency's particular decisions have been universally correct or uncontroversial, and recent years have seen FDA at the center of various political and technical controversies.

<sup>141</sup> See, e.g., Alan R. Spies et al., *Counterfeit Drugs: A Menace Keeps Growing*, 28 U.S. PHARMACIST, Jan. 15, 2003, at x, available at [http://www.uspharmacist.com/index.asp?show=article&page=8\\_1014.htm](http://www.uspharmacist.com/index.asp?show=article&page=8_1014.htm) (regarding counterfeiting and IP limitations in India and elsewhere); Peggy B. Hu & Berta Gomez, *Public Safety Jeopardized by Chinese Counterfeiters, Experts Say*, U.S. DEPT. OF STATE, INTERNATIONAL INFORMATION PROGRAMS, May 20, 2005, <http://usinfo.state.gov/eap/Archive/2005/May/20-45620.html>.

<sup>142</sup> See, e.g., WORLD HEALTH ORG., THE WORLD MEDICINES SITUATION 93, 98 (2004), available at [http://w3.who.sea.org/LinkFiles/Reports\\_World\\_Medicines\\_Situation.pdf](http://w3.who.sea.org/LinkFiles/Reports_World_Medicines_Situation.pdf) (“Fewer than one in six WHO62 Member States have well-developed drug regulation and two in six have no or very little drug regulatory capacity.”)

<sup>143</sup> Among others, Mexico, India, and China have been substantial sources of non-conforming prescription drugs imported into the U.S. See, e.g., Spies et al., *supra* note 142 (discussing counterfeiting around the globe).

<sup>144</sup> See, e.g., WORLD HEALTH ORG., *supra* note 142, at 99 (differential regulations regarding exports and “pass through” drugs in developed countries, including Germany, Netherlands, Sweden, Finland, and Switzerland); *From Test Tube to Patient, Imported Drugs Raise Safety Concerns*, FDA CONSUMER, Jan. 2006, at x, available at <http://www.fda.gov/fdac/special/testtubetopatent/imports.html> (issues with Canadian importation); U.S. DEPT. OF HEALTH AND HUMAN SERVICES TASK FORCE ON DRUG IMPORTATION, REPORT ON PRESCRIPTION DRUG IMPORTATION 60-61 (2004), available at <http://www.hhs.gov/importtaskforce/Report1220.pdf> (most countries impose lesser regulations on drugs intended for export and do not regulate drugs merely transshipped through their countries; most countries do not commit adequate resources to assure safety of exports). Canada, in particular is unprepared to assure integrity of exports to U.S. *Id.* at 62 (citing Letter from Diane C. Gorman, Assistant Deputy Minister, Health Canada, to Richard H. Carmona, Surgeon General, U.S. Public Health Service, (Jun. 1, 2004)).

origins—and they may, *by their very existence*, enhance consumer access to competing sites, located either in the regulated trade partner nation itself or elsewhere.<sup>145</sup> Hence, the existence and publication of State-sponsored importation requires that we ask how to regulate intended new channels of trade, but also how we regulate ersatz channels that may be mistaken for the intended ones. At the least, parallel trade suggests an added regulatory burden, as adequately *regulated* importation and exportation imply compliance burdens for sellers and regulators. Such burdens are liable to be most substantial in precisely the contemplated case; that is, when the trade one wishes to foster is a fluid market in *arbitrage*.<sup>146</sup>

Trade with Canada, on this account, imposes a regulatory burden even if we suppose that Canada is, for the U.S., a best-case trade partner, one with a regulatory regime that is, from our perspective, both substantial and familiar. Preliminary experience garnered by FDA suggests that the various potential problems with Canada-sourced pharmaceuticals are, even under the current legal regime, to some extent actual: Agency-sponsored enforcement efforts at the border have uncovered, among other things, misbranded products, adulterated products, and outright counterfeits, both from sources actually within Canada and from, e.g., Asian sources purporting to be Canadian.<sup>147</sup> That is not to say that the regulatory burden is in all regards intractable, merely that it is substantial and needs to be accounted for in any evaluation of the costs and benefits of parallel trade. If the benefits are few, or transitory, the costs are not likely worth paying.

#### B. CONSTRAINTS ALL THE WAY DOWN: WHAT MIGHT REGULATORY EQUIVALENCE LOOK LIKE ANYWAY?

If we were to shop around for regulatory brands, what would our shopping look like? If we were to shop only amongst equivalent regulatory regimes, how would we conceive and establish equivalence? The States that have considered and/or implemented schemes for Canadian-sourced re-importation have viewed such questions with varying degrees of scrutiny or interest. At one end of the spectrum, we may identify hastily-drafted legislation that appears to do little more than bundle the twin burdens of considering and implementing regulatory adequacy, assigning

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<sup>145</sup> See, e.g., *Examining the Implications of Drug Importation: Hearing Before the S. Comm. on the Judiciary*, 108th Cong. (2004) (statement of William K. Hubbard, Assoc. Commissioner for Pol’y and Planning, U.S. Food and Drug Admin.), available at [http://judiciary.senate.gov/testimony.cfm?id=1264&wit\\_id=3700](http://judiciary.senate.gov/testimony.cfm?id=1264&wit_id=3700) (regarding internet and other importation problems, including regulatory and safety failings of State-sponsored importation programs).

<sup>146</sup> Hence we might wish to subject to U.S. registration requirements and oversight not just a relatively small number of Canadian manufacturers, or large-scale distributors, but a very large number of smaller distributors and even retail outlets. We might *wish* to do so, the better to secure an adequate stock of *arbitrageurs*, but we might blanch at the cost.

<sup>147</sup> See, e.g., Press Release, U.S. Food and Drug Administration, Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments (Jan. 27, 2004), available at <http://www.fda.gov/bbs/topics/NEWS/2004/NEW01011.html> (regarding variously nonconforming drugs seized at import mail facilities and courier hubs); Press Release, U.S. Food and Drug Administration, FDA Test Results of Prescription Drugs from Bogus Canadian Website Show All Products are Fake and Substandard (Jul. 13, 2004), available at <http://www.fda.gov/bbs/topics/news/2004/NEW01087.html>; *Hearing Before the Subcomm. on Investigations of the S. Comm. on Governmental Affairs*, 108th Cong. (Jul. 22, 2004) (statement of John M. Taylor, III, Associate Commissioner for Regulatory Affairs, U.S. Food and Drug Administration), available at <http://www.fda.gov/ola/2004/importeddrugs0722.html>.

both, simultaneously, to State pharmacy regulators.<sup>148</sup> At the other end, perhaps, we may consider the feasibility studies undertaken by the State of Illinois prior to implementing its I-SaveRx program.<sup>149</sup> Those studies, and the program they purport to justify, have been adopted as models by several other states. Indeed, Wisconsin, Missouri, Kansas, and Vermont, have elected simply to join the Illinois importation program rather than develop their own.<sup>150</sup>

The Illinois studies are striking both for what they attempt and for what they do not. On the one hand, the studies contemplate questions of regulatory similarity for both pharmaceutical products and pharmacies, considering statutory frameworks, parallels at the level of regulatory implementation, and staffing.<sup>151</sup> At the same time, the “research method and design” of the Illinois study is, *qua* methodology, nearly impenetrable. The section on “consumer safety,” for example, “looks at the many issues surrounding patient safety ... [comparing] procedures for the manufacture, storage, and dispensing of pharmaceuticals.”<sup>152</sup> But neither the methods section nor the chapter regarding consumer safety appears to describe any technical standards for measuring consumer safety or establishing equivalence on any particular conception of equivalence.<sup>153</sup> Regulatory provisions are compared and contrasted.<sup>154</sup> Pharmacies and distributors (at least several) are visited.<sup>155</sup> A conclusion is reached: “While there are differences in the details of how the pharmacy profession is regulated, the standards of protecting the public health and safety are substantially equivalent.”<sup>156</sup>

The rationale for any particular conclusion is, however, left utterly mysterious, as is the question, which, if any, measurements were taken based on such a rationale. Similarly unclear is what Illinois intends to do by way of ongoing regulation, either on its own behalf or on behalf of other states participating in its program. Certain State pharmacy regulations are said to apply, but whether or how such application is supposed to do proxy duty for FDA’s regulatory and compliance obligation is unspecified. My own suspicion is that Illinois simply lacks the requisite resources, human and otherwise, to do the job. I want to suggest that this is a non-trivial question of institutional competence with regard to regulatory tasks that have never been handled by the States. Contract and reputational constraints may serve as *de facto* regulation in the breach, but if we were persuaded by the importance of public administrative solutions for this domain of commerce generally, we may be concerned to see private substitutes adopted on the basis of so little experience, analysis and oversight.<sup>157</sup>

<sup>148</sup> See, e.g., S.B. 410, §§ 36-43, Leg., 79th Sess. (Tex. 2005).

<sup>149</sup> See generally KAMATH, ET AL., *supra* note 48.

<sup>150</sup> See <http://www.i-saverx.net/>, welcoming the states into participation in the program.

<sup>151</sup> See KAMATH, ET AL., *supra* note 48, at 11-12 (providing an overview of research findings).

<sup>152</sup> See *id.* at 9.

<sup>153</sup> See *id.* at 8-10 (research method and design) and 11-18 (consumer fraud and safety).

<sup>154</sup> See *id.* at 16-18 (comparing Illinois pharmacy requirements with those of Ontario and Manitoba) and 38-40 (comparing text of U.S. and Canadian regulations regarding storage and warehousing of pharmaceuticals).

<sup>155</sup> See *id.* at 8.

<sup>156</sup> See *id.* at 11.

<sup>157</sup> The argument is not that private incentives to self-regulation are trivial, merely that they are not, in and of themselves, sufficient. That States would place so much faith in such a limited number of contracts, on the basis of such limited history with the relevant parties, and in the absence of developed, systematic private-side regulation, suggests to this observer more carelessness about regulatory roles than a careful rejection of them.

To the extent one is shopping for comparable regulatory brands, this may be sensible enough. An inevitably bounded comparison is carried out—certain features are compared, certain experts are consulted, and a decision is reached.<sup>158</sup> That decision may contemplate the substitution of Canadian regulation (or New Zealand, or Mexico) for FDA, just as it may contemplate the substitution of Zoloft for Prozac. To the extent one is standing in the shoes of an actual or potential regulator of cross-border trade, however, the process is puzzling if not opaque.

Implicit in the Illinois account appears to be a notion that regulatory comparisons need to take place at multiple levels of implementation, including the regulations themselves, compliance staffing, and practices on the ground.<sup>159</sup> It seems, however, that the vast majority of the regulatory comparison regards merely the language of the regulations themselves, as the study goes to some lengths in juxtaposing regulatory provisions from the two systems, but does little to compare the manner in which those provisions are implemented in fact.<sup>160</sup> What is missing, here, is any clear notion of which regulatory differences may be differences in something akin to regulatory function and which may be differences in something like the mere implementation of that function.<sup>161</sup> Clarity on this matter would be extremely useful—for the re-importation debate to be sure, but also for more general discussions of international harmonization.

With regard to criminal law, it has long been considered that the law's disincentives to crime function at multiple levels—the law as written and the law as enforced; categories of enforcement and likelihoods of enforcement; resources, both human and technical, brought to bear against crime.<sup>162</sup> With regulatory constraints on behavior, too, anything might matter to regulation *as applied*—details of the regulations themselves, regulatory guidance for industry and field personnel, compliance staffing, scheduling, training, technological resources, procedures and practices.

Differences of one sort or another may not be seen to matter, just as differences of some magnitude or another may be seen as trivial. Standards may be deemed equivalent—or close enough—on operational grounds. They may, that is, be differences *merely in the implementation* of whatever regulatory function has been deemed important. Those grounds do, however, need to be identified and defended, if regulatory regimes are to be deemed “substantially equivalent” by something more than executive fiat.<sup>163</sup> But prior to identifying, and justifying, a given level of regulatory precision, we might start with a more basic notion of equivalence: if

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<sup>158</sup> There is a burgeoning literature regarding the application of concepts of heuristics and bounded search to legal problems. See, e.g., Owen D. Jones, *The Evolution of Irrationality*, 41 JURIMETRICS 289 (2001), BEHAVIORAL LAW AND ECONOMICS (Cass Sunstein, ed., 2000). Empirical investigations of, e.g., bounded trust and bargaining games are discussed at Vernon Smith, *Experimental Methods in Economics*, in ENCYCLOPEDIA OF COGNITIVE SCIENCE 2003, at 1070-79 (2003), available at <http://www.neuroeconomics.net/pdf/materials/455.pdf>.

<sup>159</sup> See KAMATH, ET AL., *supra* note 48, at 38 (regarding Good Manufacturing Practice regulations and quality control).

<sup>160</sup> See *id.* at 40-44 and appendices A and B (comparing U.S. and Canadian regulatory requirements for warehousing and storage of pharmaceuticals).

<sup>161</sup> Notions of functional decomposition and implementation across multiple levels of explanation have been explored more fully in the cognitive and biological sciences than they have in this domain.

<sup>162</sup> See generally Gary S. Becker, *Crime and Punishment: An Economic Approach*, 76 J. POL. ECON. 169 (1968); ESSAYS IN THE ECONOMICS OF CRIME AND PUNISHMENT (Gary S. Becker & Willam M. Landes, eds. 1974).

<sup>163</sup> KAMATH, ET AL., *supra* note 48, at 11.

anything *might* matter, then to first approximation, regulatory equivalence, like regulatory responsibility, goes all the way to the bottom.

#### V. DOWN THE ROAD: TRADE, REGULATION, AND HARMONIZATION ON A LARGER SCALE

The debate about re-importation continues apace. Within the U.S., the prominence of Canada in the debate is something of a red herring. There are very good legal and economic reasons why pharmaceuticals are to some extent cheaper in Canada. We may dispute the *extent* to which such reasons explain or justify cross-border price disparities. We may dispute, too, the extent to which it would be in the interest of the U.S. to approach Canadian pricing policy or price levels. We cannot, however, think that Canada holds much promise as a supplier of pharmaceuticals adequate in scale to substantially lower U.S. drug prices. The Canadian market, in its present form, is simply too small to fulfill that function, and elimination of the regulatory border from the U.S. side may very well make it smaller. We have seen that nascent attempts by several of the States to circumvent federal authority on importation have, already, implicated public and private steps, on both sides of the border, to reduce cross-border pharmaceuticals arbitrage. We have seen too, that nascent State-based re-importation schemes have already had to look further and further abroad for sources of imports, despite the fact that only a small minority of eligible citizens have sought to participate in those schemes.

I have argued that there is another problem with Canadian-sourced imports for U.S. pharmaceuticals consumers, a safety problem. As FDA has pointed out, Canadian-sourced imports have been found variously non-conforming with regard to U.S. drug regulations; and imports purportedly sourced in Canada have been found to come from elsewhere entirely.<sup>164</sup> That latter fact should give us special pause, given the large number of conspicuously inadequate regulatory regimes across the globe.<sup>165</sup> The issue is not that Canadian regulation of pharmaceuticals safety is, *in itself*, inferior to U.S. regulation. The issues are, rather, (a) that we may fail in several ways to reap the benefits of Canadian regulation when we seek Canadian sources and (b) that there is an imperfect regulatory fit between the two systems. In brief, regulatory adequacy is context sensitive, and equally defensible standards may fail to be either commensurable or transferable across the relevant contexts. That is a problem because this market requires regulation, and it is a problem to the extent that this market requires regulation. To the extent that a comprehensive regulatory scheme is critical from public and private health perspectives—critical, that is, to the proper functioning of the pharmaceuticals market—questions about regulatory adequacy become central in domestic health policy, and in international trade and IP policy.<sup>166</sup>

Market, healthcare, and regulatory differences between the two nations impose special administrative costs on both sides of the border. Differences in labeling, packaging, dosing, and distribution do not necessarily pose intractable barriers to trade. But if we must stand in the shoes of the pharmaceuticals regulator to make

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<sup>164</sup> See, e.g., Press Release. U.S. Food and Drug Administration, *supra* note 148; Press Release, U.S. Food and Drug Administration, *supra* note 148. Links to these and other pages available at <http://www.fda.gov/importeddrugs> (last visited Nov. 28, 2005).

<sup>165</sup> See *supra* text accompanying note 143 (WHO regards drug regulation as systematically inadequate in most nations).

<sup>166</sup> See *supra* text accompanying notes 107-141.

either market, or trade between them, function as it should, then we must account for such differences one way or another. We need to begin with a thick, multi-layered comparison of the two systems, identify asymmetries and gaps between them, and decide, on some systematic grounds: which areas of concern matter (and which do not), how much the concerns matter, and what might be done, on a cost-justified basis, to manage them. This simply has not been done and its doing is, as I've argued, unlikely to be worthwhile for either the United States or Canada.

If this is fundamentally an administrative problem, concerns about Canada may fruitfully be considered in light of other, more systematic, attempts at regulatory integration. Impediments to trade generally call for justification and, our concerns about parallel trade notwithstanding, the globalization of drug development, production, marketing, and distribution, do not obviously benefit from the variation in regulatory schema we observe around the globe. Consumers—patients all—do not obviously benefit from them either.<sup>167</sup> To that end, we might consider what, e.g., EU harmonization may have to offer as a model of regulatory integration.

The European integration process may be the best model of a large scale, directed program of market and regulatory integration available.<sup>168</sup> Certainly it is the most ambitious, ranging over diverse areas of industrial and trade policy, health policy, and human rights in deep ways, and incorporating significant legislative, regulatory, compliance, and judicial functions.<sup>169</sup> EU pharmaceuticals regulation, via Community legislation and the regulatory activities of the EMEA, is surely the most significant program of pharmaceuticals and biologics regulatory integration seen to date. That integration is neither seamless nor complete.<sup>170</sup>

The EU has provided, among other things, a unifying statutory framework for medicines, a centralized regulatory agency, and a centralized approval process for medicines.<sup>171</sup> The EU has also provided for parallel trade, in drugs, among member states.<sup>172</sup> Less settled is the extent to which implementation of the European scheme will achieve either real regulatory integration or the growth of a single European market. Thus far, EU integration remains incomplete in several ways. That is significant to the extent we might look upon the EU as a model of regulatory

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<sup>167</sup> Diversity in regulatory requirements is not pointless either. To the extent that decisions regarding, e.g., drug safety and efficacy involve complex risk assessment and the balancing of risks and benefits, disparate administrative decisions—and, indeed, regulatory standards—may be equally defensible within or across markets. We may, in fact, expect significant variation in standards across nations presenting substantially different economic and health conditions.

<sup>168</sup> For general background, see PAUL CRAIG & GRÁINNE DE BÚRCA, *EU LAW: TEXT, CASES, AND MATERIALS* (3rd ed. 2003), especially chapter 1, the Development of European Integration.

<sup>169</sup> The scope of this project defies any single citation. For general background, see *id.* Important defining documents include, e.g., European Union Treaty (Maastricht) (1992); Treaty of Rome (1957) (seeds of EU providing for, e.g., competition and free movement of goods), Convention on Human Rights and Biomedicine (Council of Europe) (1996); Brussels Convention on Jurisdiction and Enforcement of Judgments in Civil and Commercial Matters (1968); and the European Patent Convention (1973). Current EU legislation may be found <http://dg3.eudra.org/eudralex/index.html>.

<sup>170</sup> For an overview of relevant issues, see *REGULATING PHARMACEUTICALS IN EUROPE: STRIVING FOR EFFICIENCY, EQUITY, AND QUALITY* (Elias Mossialos, et al. eds. 2004).

<sup>171</sup> See Council Directive 2004/27, 2004 O.J. (L 136) 34 (EC) (amending Council Directive 2001/83/EC on the Community code relating to medicinal products for human use (Act of the EU regarding pharmaceutical products)). An overview of the European Medicines Agency (EMA) may be found at <http://www.emea.eu.int/htms/aboutus/emeaoverview.htm> (last visited April 4, 2006).

<sup>172</sup> See Case 15/74, *Centrafarm v. Sterling Drug*, 1974 E.C.R. 1147. For a discussion of the emergence of the principle, see Cornish, *supra* note 20, at 17-19.

integration and it is significant to the extent we might look to it as another source of imports.

The EU is not, of course, a fixed limited entity. The population of member states has grown since the inception of the Union; new member states have been admitted recently; and the Union may well expand further in the near future.<sup>173</sup> In addition, the most recent EU medicines legislation has not yet been fully implemented by all member states and newer member states have yet to assimilate fully their regulatory schemes.<sup>174</sup> What is more, if we take seriously the notion that real regulatory equivalence depends on equivalence *across* levels of implementation—beginning with a statutory and code framework, but running through fine institutional structures and competencies, compliance resources, etc.—then we must recognize that the promise of integration is, at least in the near term, limited to a certain degree of high-level policy coordination. The likelihood that medicines regulation will soon mean the same thing—on the ground—from Britain, through Greece, to Turkey seems slight, to say the least.

Regulatory difference across the union explains a certain lack of uniformity—and indeed a certain degree of strategic game playing—in the approval of medicines in Europe.<sup>175</sup> New pharmaceutical medicines in the EU may take one of two principal approval pathways—that of the centralized approval procedure or that of the mutual recognition procedure.<sup>176</sup> Under centralized approval, application is made to the EMEA itself and approval for marketing, once granted, is valid in all member states.<sup>177</sup> Under mutual recognition, on the other hand, a manufacturer submits its product to the scrutiny of an individual member state's authorizing authority and then seeks, through the EMEA, the extension of marketing authority to one or more additional member states.<sup>178</sup> In the event that a named member state declines to recognize the approval in question, the EMEA plays the role of arbitrator.<sup>179</sup>

Most new drugs now receive authorization via the centralized procedure.<sup>180</sup> Centralized approval does several things, but it does not erase heterogeneity of regulatory scrutiny across the Union. It does not, for example, impose quite the

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<sup>173</sup> The EU may be traced to the creation of, among other things, the European Economic Community with the signing of the Treaty of Rome, by six nations, in 1957. Ten new member states were admitted in 2004. For a graphic representation of EU membership, which currently includes 25 member states and contemplates four "applicant states" (including Bulgaria, Croatia, Romania, and Turkey), see European Governments On-Line, European Union Member States, [http://europa.eu.int/abc/governments/index\\_en.htm](http://europa.eu.int/abc/governments/index_en.htm) (last visited Nov. 27, 2005). For a brief overview of the history of the EU, see The History of the European Union, [http://europa.eu.int/abc/history/index\\_en.htm](http://europa.eu.int/abc/history/index_en.htm) (last visited, Nov. 27, 2005).

<sup>174</sup> Contact EMEA for latest information on implementation.

<sup>175</sup> See generally Antoine Culliver, *The Role of the European Medicines Evaluation Agency in the Harmonisation of Pharmaceutical Regulation*, in PHARMACEUTICAL MEDICINE, BIOTECHNOLOGY, AND EUROPEAN LAW (Richard Goldberg & Julian Lonbay eds., 2000); Silvio Garattini & Vittorio Bertelé, *The Role of the EMEA in Regulating Pharmaceutical Products*, in REGULATING PHARMACEUTICALS IN EUROPE: STRIVING FOR EFFICIENCY, EQUITY, AND QUALITY 2 (Elias Mossialos et al., eds. 2004)..

<sup>176</sup> See Council Regulation 2309/93, Annex, 1993 O.J. (L214) 24 (EC). See generally Culliver, *supra* note 175.

<sup>177</sup> See Council Regulation 2309/93, *supra* note 177, at 24.

<sup>178</sup> See *id.*

<sup>179</sup> See Culliver, *supra* note 175, at 143-144.

<sup>180</sup> Most new pharmaceutical drugs approved within the EU are approved via the centralized procedure; *all* new biological drugs must be approved through the centralized procedure. Council Regulation 2309/93, *supra* note 177.

same authorization strictures on all submissions.<sup>181</sup> At least in certain regards, the EMEA is not so much a full-fledged (or fully-staffed) regulatory agency, but a coordinating agency for the diverse authorities of the various member states.<sup>182</sup> Whereas, for example, U.S. applications for the authority to market new drugs inevitably proceed through the FDA, which issues, for example, an investigational new drug exemptions permitting the conduct of clinical trials and which oversees the progress of those clinical trials, the EMEA farms out the lion's share of its approval oversight to the authorizing authorities of the individual member states.<sup>183</sup> Thus, the authorizing authorities of individual member states stand in the shoes of the EMEA.<sup>184</sup> That results in several loci of strategizing. First, manufacturers may prefer to seek the regulatory scrutiny of one agency rather than another. Second, just as U.S. regulation depends, in part, on fees generated by applications themselves, so too, does European regulation.<sup>185</sup> As a consequence, certain agency problems may be magnified under the European regulatory scheme and some have observed that both the central authority and the authorities of the various member states are interested parties whose interests may diverge when it comes to the question *which* regulatory pathway a given new drug will face.<sup>186</sup>

Earlier, I presented familiar arguments as to why we ought to seek administrative solutions to certain sorts of problems and why, for a sub-class of such problems, we ought to seek solution via government administration. I noted that such arguments were not developed without a degree of caution, as administrative solutions posed their own agency problems and as government administration posed further problems still. All such problems impose costs on any organizational endeavor. With regard to any particular administrative problem (or class of problems), attention then turns to the means of minimizing such costs. What should not be supposed, without examination, is that any particular administrative solution is efficient or even functional.

The impetus towards regulatory harmonization is plain enough. Technical and institutional expertise may be pooled, reducing certain total and average administrative costs, while at the same time reducing development, manufacturing, marketing, and distribution costs for manufacturers of products that are intended for global markets. At the margin, we should expect price to be reduced and supply increased, and at least some pharmaceutical products may exist at that margin.

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<sup>181</sup> See Garattini & Bertelé, *supra* note 176, at 84-89.

<sup>182</sup> Culliver, *supra* note 175, at 146 ("It is not a Food and Drug Administration for Europe, but rather it is a 'virtual agency,' interfacing with its partners without dismantling their structures.")

<sup>183</sup> See Garattini & Bertelé, *supra* note 175, at 84-86 (regarding procedures for evaluating approval dossiers).

<sup>184</sup> Garattini and Bertelé report that, of the two "rapporteurs" required under the centralized procedure one is typically suggested by the EU regulator (specifically, the Committee for Proprietary Medicinal Products) and one is typically suggested by the manufacturer. See *id.* at 84.

<sup>185</sup> Indeed, EU approval depends more heavily on user fees than does the FDA. See *id.* at 87-88 (reporting majority funding from user fees in EU versus only 15% in U.S., under the Prescription Drug User Fee Act). In the U.S., fees are required of each "human drug application" by statute. See 21 U.S.C. § 379g(1) (2006); U.S. FOOD AND DRUG ADMINISTRATION, CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)/CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER), GUIDANCE FOR INDUSTRY: SUBMITTING SEPARATE MARKETING APPLICATIONS AND CLINICAL DATA FOR PURPOSES OF ASSESSING USER FEES 1, available at <http://www.fda.gov/cber/gdlns/appsf.pdf>.

<sup>186</sup> See Garattini & Bertelé, *supra* note 175, at 87-89; Elias Mossialos et al., *supra* note 107, at 8.

Hence we observe not just the European integration program, but, for example, the considerable progress of the International Conference on Harmonization.<sup>187</sup>

At the same time, we cannot help but notice that international administration amplifies certain familiar agency costs and creates, perhaps, its own distinctive ones. Monitoring costs, for example, are liable to increase with the scale of the regulatory endeavor. They are also liable to increase as administration ranges over increasingly diverse populations and is implemented through increasingly diverse regulatory mechanisms and systems. What I want to suggest regarding a proto-integrated Europe is this: the extent to which the harmonization of regulatory requirements and the centralization of administrative authority are truly practicable remains to be seen.

The particular architecture of European drug regulation is, at least in some regards, at odds with the commitment to open trade based on common regulatory standards.<sup>188</sup> That suggests, at the very least, that we be wary of parallel trade in pharmaceuticals with the Union as a whole. And to the extent that parallel trade within the EU is preserved, it suggests that we be wary of parallel trade with any particular member state, even as certain of those states have well established and familiar medicines regulation. Parallel trade with the United Kingdom, for example, would pose many of the same concerns raised by proposals for parallel trade with Canada, and then some; the considerable resources of the Medicines and Healthcare Products Regulatory Agency notwithstanding. Establishing administrative coordination with Britain imposes one set of costs, and uncertainties about our ability to cabin that coordination, against issues raised elsewhere in Europe, another. The following generality may be observed: expanding the network of parallel trade partners may expand the benefits of price competition; but expanding the network is liable, at the same time, to amplify the market's natural risks and the administrative costs of managing them.

In the meantime, we have a vibrant laboratory for our general questions about balancing open markets and regulatory concerns for drugs, a laboratory we may prefer to the motley of hastily conceived and implemented parallel-trade programs seen in many U.S. states. Experimentation in the states does not, after all, need to be experimentation in *our* states. As with all experimentation, the demonstration lies in the data—yet to be developed—but the worth of the demonstration lies centrally in the controls. We must remember *all* the relevant variables in our price, property, trade, and health problem. There are, as I hope to have shown, quite a few.

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<sup>187</sup> The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is an ongoing public/private conference between regulatory agencies and pharmaceutical trade associations in the U.S., the E.U., and Japan. ICH projects include, the Common Technical Document (regarding a standard format for the submission of drug safety and efficacy information) and the Medical Dictionary for Regulatory Activities (MedRA). ICH documents and other information may be found at Welcome to The Official Website for ICH, <http://www.ich.org/cache/compo/276-254-1.html> (last visited April 5, 2006). For an overview of recent FDA-ICH activity, see FDA's Center for Drug Evaluation and Research, *International Activities*, <http://www.fda.gov/cder/audiences/iact/iachome.htm#ICH> (last visited April 5, 2006).

<sup>188</sup> See Garattini & Bertelé, *supra* note 175, at 86-87 (discussing conflicts between health and industrial policy accentuated by institutional location of EMEA in European Commissions General Directorate of Enterprises rather than the Public Health Directorate).