

Bitter Biopharmaceuticals: Biologic Counterfeiting and Supply Chain Concerns

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Pharmaceutical counterfeiting is a growing area of public safety and national security concern. Biological medications are a growing portion of counterfeit medicines due to the high cost and opportunities for profit from these innovative drugs. Biologics are a unique target for counterfeiters in international commerce presenting unique hazards over traditional, more stable, pills. This Article explores the international biopharmaceutical supply chain and the regulatory weaknesses that compromise public health.

I. INTRODUCTION

Pharmaceutical counterfeiting is a gravely important problem due to the public safety risks of a compromised medicine supply chain. This Article will explore how biopharmaceuticals, innovative and costly medicines, have a heightened risk of counterfeiting and the paths by which counterfeits end up in doctors' offices. Following a test case exploring the distribution supply chain, we will see that lax efforts to police the gray market of pharmaceutical parallel imports have compromised patient safety in the United States (U.S.), which has a robust regulatory and drug safety regime.

The international medicinal supply chain is a complex network of suppliers, distributors, and doctors helping patients and making a living in a non-harmonized international marketplace. Prescription drugs may be manufactured abroad and pass through many nations with different standards before reaching critically ill patients. Without a unified global regulatory system and deterrent penalties, criminals take advantage of a high priced marketplace compromising the security of the drug supply system.

Using the biologic drug Avastin as the test case, this Article will look at the statutory manufacturing and importation schemes of the U.S., Canada, European Union (E.U.), and Turkey to see how a counterfeit drug passed through many hands before administration to American cancer patients. The response to that incident is weighed and recent legal developments analyzed. Finally, this Article will propose recommendations for monitoring and securing the pharmaceutical supply chain to target regulatory weaknesses.

II. COUNTERFEITING IN PHARMACEUTICALS

The World Health Organization (WHO) previously estimated that 10% of the global pharmaceutical market is counterfeit.¹ However, the WHO

1. Bill Berkot, *Fake Avastin shows little protection of drug supply*, REUTERS (Mar. 12, 2012, 1:39 PM), <http://www.reuters.com/article/us-avastin-drug-fake-idUSBRE82B0YY20120312>.

warns against reporting such shocking figures because there are many variables in assessing the extent of pharmaceutical counterfeiting.² The pervasiveness of counterfeits in the marketplace varies widely by region.³ Industrial nations have less than 1% counterfeit penetration.⁴ The problem can reach 30% or more of the marketplace in developing countries.⁵ Counterfeiting is likely underestimated and often goes unreported due to difficulties in measuring the problem.⁶ Counterfeiters actively conceal their involvement and cover up crimes hindering assessment.⁷

Criminals driven by financial gain are involved in all facets of the illicit medicine supply chain, including manufacturing and distribution.⁸ The international regulatory framework is also ill equipped to protect against terrorist organizations playing a role in the marketplace.⁹ The ease of entry into the marketplace and opportunity to make large profits encourages counterfeiters.

This Article is concerned with medication counterfeits and tampered medications rather than intellectual property misappropriation, also commonly identified as a counterfeiting issue. Awareness of intellectual property issues plays a role in identifying counterfeits. As this Article will show, misuse of trademark and packaging standards raised red flags for practitioners who attempted further investigation of medication that turned out to be fake. The labeling was a telltale giveaway of counterfeiting and easily detectable as the fake drugs moved through the supply chain.

2. INT'L MEDICINAL PRODUCTS ANTI-COUNTERFEITING TASKFORCE [IMPACT], COUNTERFEIT MEDICINES: AN UPDATE ON ESTIMATES (Nov. 15, 2006), <http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf>.

3. *Id.* (Within geographic regions, there may also be large differences in urban versus rural counterfeit rates.).

4. CTR. FOR DISEASE CONTROL AND PREVENTION [CDC], COUNTERFEIT DRUGS, <http://www.cdc.gov/features/counterfeitdrugs/> (last updated Apr. 7, 2014).

5. *Id.*

6. See Tim K. Mackey et al., *Counterfeit Drug Penetration into Global Legitimate Medicine Supply Chains: A Global Assessment*, 92 AM. J. TROP. MED. HYGIENE 59, 59–60 (2015).

7. IMPACT, *supra* note 2.

8. INTERPOL, PHARMACEUTICAL CRIME AND ORGANIZED CRIMINAL GROUPS: AN ANALYSIS OF THE INVOLVEMENT OF ORGANIZED CRIMINAL GROUPS IN PHARMACEUTICAL CRIME SINCE 2008, at 5 (2014).

9. See Douglas T. Cannon, *War Through Pharmaceuticals: How Terrorist Organizations are Turning to Counterfeit Medicine to Fund Their Illicit Activity*, 47 CASE W. RES. J. INT'L L. 343 (2015) (discussing how terrorists may use the lax pharmaceutical regulatory environment as a funding opportunity).

“We should not get confused by so many other terms, which have hindered the movement in councils of discussion,” said Joel Breman, senior scientist emeritus at the National Institute of Health.¹⁰ There is currently no uniform international definition of a counterfeit drug.¹¹ Previously, the WHO defined a counterfeit drug as “a pharmaceutical product whose origin and/or identity specifications have been deliberately and fraudulently modified.”¹² Today, the WHO encourages using the expression Substandard, Spurious, Falsely labeled, Falsified and Counterfeit (SSFFC) Medical Products to describe the range of goods that endanger public health.¹³ U.S. law defines counterfeit drugs as those sold under a product name without proper authorization.¹⁴ Counterfeit products may include products without the active pharmaceutical ingredient (API), with an insufficient or excessive quantity of the API, containing the wrong API, or with unlicensed packaging.¹⁵

Under U.S. law, a counterfeit drug can be a drug or its packaging with misleading features or falsely purporting to be the licensed and genuine product.¹⁶ Misrepresentation of drugs is a broad category taking many forms. Complete fakes are counterfeits manufactured with no genuine medicinal components or API.¹⁷ This Article explores the counterfeiting incident where the injectable cancer drug Avastin was a complete counterfeit containing no therapeutic ingredient benefiting cancer victims.¹⁸ Patients receiving it experienced severe reactions; they began to shake and needed

10. Bea Perks, *Pharmaceutical Fakes: A Dangerous Pandemic*, PHARMACEUTICAL JOURNAL (May 21, 2015), <http://www.pharmaceutical-journal.com/news-and-analysis/features/pharmaceutical-fakes-a-dangerous-pandemic/20068533.article>.

11. WORLD HEALTH ORG. [WHO], SSFFC – FREQUENTLY ASKED QUESTIONS, http://www.who.int/medicines/regulation/ssffc/faq-ssffc_11-18/en/index4.html (last visited Nov. 11, 2016).

12. UNITED NATIONS INTERREGIONAL CRIME AND JUSTICE RESEARCH INST. [UNICRI], ORGANIZED CRIME STRATEGIES IN THE PRODUCTION AND TRADE OF COUNTERFEIT MEDICINES 2, http://www.unicri.it/topics/counterfeiting/medicines/savemed/D7.1_OC_Strategies_2013.pdf (last visited Nov. 25, 2016).

13. WHO, *supra* note 11; *see also* Gian Luca Burci, *Public Health and “Counterfeit” Medicines: The Role of the World Health Organization*, AM. SOC’Y OF INT’L L. (Jan. 11, 2013), <https://www.asil.org/insights/volume/17/issue/2/public-health-and-%E2%80%9Ccounterfeit%E2%80%9D-medicines-role-world-health-organization> (distinguishing the public health issue of counterfeit drugs from traditional intellectual property violations).

14. U.S. FOOD AND DRUG ADMIN. [FDA], COUNTERFEIT DRUGS QUESTIONS AND ANSWERS, <http://www.fda.gov/Drugs/DrugSafety/ucm169898.htm> (last updated Apr. 27, 2011).

15. *Id.*

16. 21 U.S.C. § 321 (2006).

17. *See* Maria Nelson, Michelle Vizurraga & David Chang, *Counterfeit Pharmaceuticals: A Worldwide Problem*, 96 TRADEMARK REP. 1068, 1073–74 (2006).

18. Christopher Weaver & Jeanne Whalen, *How Fake Cancer Drugs Entered the U.S.*, WALL ST. J. (July 20, 2012, 3:02 PM), <http://www.wsj.com/articles/SB10001424052702303879604577410430607090226>.

to be disconnected from the sham treatment.¹⁹ The container was also phony, bearing the Turkish brand name *Alzutan* with English language packaging, a combination not seen in the genuine pharmaceutical.²⁰

There are also tampered fakes having a genuine component, such as the package or label, but are altered in another way.²¹ Tampered fakes may be diluted drugs that are less potent than the label asserts.²² A re-labeled counterfeit may contain authentic drug, but with the expiration date altered, misrepresenting the drug's safety and effectiveness.²³ In January 2013, police in Colombia arrested 21 pharmaceutical counterfeiting suspects.²⁴ A total of 89,754 medications were seized from an organized crime group falsifying the expiration dates and batch numbers.²⁵ This type of counterfeiting undermines the quality control system that ensures effectiveness of drug products.

Through another type of counterfeiting, diverted fakes illegally enter the pharmaceutical market through theft or diversion.²⁶ Criminal groups specializing in robbery steal and resell medication to secondary distributors and wholesalers, or, many times, directly to pharmacists.²⁷ A common example of diversion is antimalarial medicine in African markets, where diversion by theft of legitimate medication can lead to serious stock shortages, endangering public health in countries with high numbers of infected patients.²⁸

Counterfeiting pharmaceuticals is an attractive and lucrative opportunity for criminals. For organized crime groups involved in pharmaceutical

19. John Roth, *Counterfeit Drugs: Prosecuting the Profiteers*, FDA VOICE (July 15, 2013), <http://blogs.fda.gov/fdavoices/index.php/2013/07/counterfeit-drugs-prosecuting-the-profiteers-protecting-the-public-health/>.

20. Ben Hirschler, *New Batch of Fake Avastin Reached U.S. via Britain* (Apr. 5, 2012, 2:54 AM), <http://www.reuters.com/article/2012/04/05/us-avastin-fake-idUSBRE83407D20120405>.

21. See Nelson, Vizurraga & Chang, *supra* note 17, at 1073–74.

22. CMS, *The Problem—The Patent and Brand Thief* (Jan. 6, 2005), <http://www.cms-cmck.com/newsmedia/news/newsdetail/pages/default.aspx?PublicationGuid=1e9640c5-7435-47d3-a5f5-d0551ef0f487>.

23. *Id.*

24. INTERPOL, *supra* note 8, at 8.

25. *Id.*

26. *Id.* at 13.

27. *Id.* (for example, in late 2011, Brazil's Internal Affairs Division seized 61 boxes of stolen medications at legitimate clinics in Sao Paulo).

28. *Id.*

wrongdoing, there is often no need to resort to violence.²⁹ Unlike criminals dealing exclusively with illegal drugs such as heroin and cocaine, counterfeiting medicine allows counterfeiters to keep a low profile and avoid law enforcement authorities.³⁰

Some countries face legislative challenges to thwarting pharmaceutical crime, as few countries possess specific legislation to target this type of counterfeiting crime.³¹ Furthermore, many countries indicate that poor penalties are a contributing factor for the proliferation of criminal networks.³² For example, in the U.S., distributors, doctors, and their staff may receive only probation for providing unapproved drugs and knowingly risking the health and safety of patients trusting them to give quality care.³³

Criminal groups involved in medicine counterfeiting vary in their level of proficiency. Poor drug imitation packaging may include misspellings and a combination of different languages.³⁴ High-quality counterfeits are more difficult to distinguish from genuine versions.³⁵ The more sophisticated the product, the more sophisticated the criminals responsible for the forgery. For example, an international organized crime group based in the U.K., and dismantled in late 2011, produced counterfeit erectile dysfunction tablets, physically identical to the genuine drug, also containing API.³⁶

The Pharmaceutical Security Institute (PSI) manages a secure database recording incidents of counterfeiting, theft, and illegal diversion of pharmaceutical products worldwide.³⁷ The number of counterfeiting incidents recorded has risen nearly 60% over the last decade.³⁸ As drug counterfeiting continues to set records, biologic counterfeiting has room to grow.³⁹

29. *Id.* at 12.

30. *Id.* (discussing how the comparatively low level of violence lowers barriers to entry).

31. *Id.* at 16.

32. *Id.*

33. See Press Release, FBI, Greenville Oncologist and Practice Manager Sentenced for Violating Food, Drug, and Cosmetic Act (June 12, 2014), <https://www.fbi.gov/knoxville/press-releases/2014/greenville-oncologist-and-practice-manager-sentenced-for-violating-food-drug-and-cosmetic-act>.

34. See Peter Spinella, *Russian Ex-Cop Runs \$670,000 Counterfeit Drug Factory at Home*, MOSCOW TIMES (Feb. 10, 2012), <http://www.themoscowtimes.com/business/article/ex-cop-runs-bogus-drug-plant-at-home/452818.html>.

35. INTERPOL, *supra* note 8, at 12.

36. *Id.*

37. PHARMACEUTICAL SECURITY INST., COUNTERFEIT SITUATION, <http://www.psi-inc.org/counterfeitsituation.cfm> (last visited Feb. 2, 2016).

38. See generally Thomas T. Kubic, *Beer Cooler Biologics: The Dangers of Counterfeit Drugs*, THE POLICE CHIEF, Aug. 2008, at 44–48.

39. Patricia Van Amum, *Tracking Growth in Biologics*, 37 PHARMACEUTICAL TECH. (2013), <http://www.pharmtech.com/tracking-growth-biologics>; see also Cormac Sheridan, *Bad Medicine*, 25 NATURE BIOTECHNOLOGY 707, 707 (2007), <http://www.nature.com/nbt/journal/v25/n7/full/nbt0707-707.html>.

Increased demand for high priced biological treatments will surely attract more attention from counterfeiters adept at profiting off public demand for new pharmaceutical advancements.

III. BIOPHARMACEUTICALS

A class of treatments called biopharmaceuticals, or biologics, currently drives biomedical research and development.⁴⁰ Biologics are responsible for breakthroughs in treating cancer, HIV, and other illnesses.⁴¹ Biologics are pharmaceuticals made from natural sources including vaccines, gene therapies, antibodies, and blood products.⁴² Biologic treatments differ from traditional drugs, which are chemically synthesized.⁴³

In the U.S., the Food and Drug Administration (FDA) regulates manufacture and labeling of biologics.⁴⁴ Like all medications in the U.S., biological products go through FDA review prior to market approval.⁴⁵ The time between discovery of a new drug and the moment that drug reaches the consumer takes an average of 12 to 13 years.⁴⁶ On average, only one or two substances developed in the laboratory will successfully pass all stages of development to become a marketable medicine.⁴⁷

The ultimate high cost of treatment reflects the difficulties of the manufacturing process and the complexity of biologic products.⁴⁸ The average cost of creating a new biological entity in 2012 was \$1.5 billion.⁴⁹

40. U.S. FOOD AND DRUG ADMIN. [FDA], WHAT IS A BIOLOGICAL PRODUCT?, <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194516.htm> (last updated Aug. 20, 2015).

41. Michael C. Barnes & Stacey L. Worthy, *Applying Lessons from the Opioid Abuse Epidemic to Protect Consumers from Gray Market Biologics*, 29 NOTRE DAME J. L., ETHICS & PUB. POL'Y 375, 377 (2015), <http://scholarship.law.nd.edu/cgi/viewcontent.cgi?article=1753&context=ndjlepp>.

42. U.S. FOOD AND DRUG ADMIN. [FDA], *What are "Biologics" Questions and Answers*, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm> (last updated Aug. 5, 2015).

43. *Id.*

44. 21 C.F.R. § 600 et seq. (2015).

45. 21 U.S.C. § 355 (2015).

46. EUROPEAN FEDERATION OF PHARMACEUTICAL INDS. AND ASS'NS [EFPIA], THE PHARMACEUTICAL INDUSTRY IN FIGURES 6 (2014), http://www.efpia.eu/uploads/Figures_2014_Final.pdf.

47. *Id.*

48. Andrew Wasson, *Taking Biologics for Granted? Takings, Trade Secrets, and Off-Patent Biological Products*, DUKE L. & TECH. REV. ¶ 1, ¶ 2 (2005), <http://www.law.duke.edu/journals/dltr/articles/2005dltr0004.html>.

49. EFPIA, *supra* note 46, at 6.

Treatments of biologic drug Avastin could cost cancer patients over \$100,000 per year in 2008.⁵⁰ In 2010, some biologics cost over \$2,000 per dose.⁵¹ Drug companies have a tremendous interest in protecting research and development investments and the goodwill of their brands with such large stakes involved.⁵² The market for biologics is growing rapidly.⁵³ Projections indicate biologics will make up 20% of the pharmaceutical market by 2017.⁵⁴ Increasing demand for the high-priced medicinal products makes the biologics market susceptible to counterfeiters seeking to exploit a vulnerable and desperate patient population.

The WHO advises that quality assurance of biological medicines is necessary.⁵⁵ Safety considerations particular to biopharmaceuticals involve the biological nature of the raw materials used, the manufacturing process, and the tests and methods safeguarding production consistency.⁵⁶ It is problematic to detect counterfeit biologics because injectable versions may consist of a white powder similar to legitimate medicine in smell, taste, or appearance.⁵⁷ Biologics are less stable than chemical pharmaceuticals.⁵⁸ There is a greater risk of instability, ineffectiveness, and contamination when biologics are not stored properly.⁵⁹ They are prone to degradation

50. Leigh Purvis, *Biologics in Perspective: A Case for Generic Biologic Drugs*, AARP PUBLIC POL'Y INST. 1 (2009), http://assets.aarp.org/rgcenter/health/fs155_biologics.pdf (Biologic drug sales in 2007 totaled \$75 billion. See chart for Avastin and top biologic sales compared to the cost of research and development.); Gina Kolata & Andrew Pollack, *Costly Cancer Drug Offers Hope, but Also a Dilemma*, N.Y. TIMES (July 6, 2008), http://www.nytimes.com/2008/07/06/health/06avastin.html?_r=0.

51. Hutton et al., *Switching to Less Expensive Blindness Drug Could Save Medicare Part B Over \$18 Billion Over a Ten-Year Period*, 33 HEALTH AFFAIRS 931, 931 (2014), http://www.ascrs.org/sites/default/files/1453_001.pdf; DEPT. OF HEALTH AND HUMAN SERVICES OFFICE OF INSPECTOR GENERAL, *MEDICARE PAYMENTS FOR DRUGS USED TO TREAT WET AGE-RELATED MACULAR DEGENERATION 11* (2012), <http://oig.hhs.gov/oei/reports/oei-03-10-00360.pdf> (contractor's payments differed by as much as 28%).

52. See Cormac Sheridan, *Bad Medicine*, 25 NATURE BIOTECHNOLOGY 707, 707 (2007), <http://www.nature.com/nbt/journal/v25/n7/full/nbt0707-707.html>.

53. Simon King, *The Best Selling Drugs Since 1996 - Why AbbVie's Humira Is Set To Eclipse Pfizer's Lipitor*, FORBES (July 15, 2013, 8:34 AM), <http://www.forbes.com/sites/simonking/2013/07/15/the-best-selling-drugs-since-1996-why-abbvies-humira-is-set-to-eclipse-pfizers-lipitor/>.

54. See IMS INSTITUTE FOR HEALTHCARE INFORMATICS, *THE GLOBAL USE OF MEDICINES: OUTLOOK THROUGH 2017 9* (2013), <http://www.quotidianosanita.it/allegati/allegato1501906.pdf>.

55. Kubic, *supra* note 38.

56. *Id.*

57. Ravi Kalyanaraman et al., *Screening and Detecting Counterfeit Biologics Drugs*, 2 BIOPHARMA ASIA 58, 58 (2013).

58. Thomas Morrow & Linda Hull Felcone, *Defining the Difference: What Makes Biologics Unique*, 1 BIOTECHNOLOGY HEALTHCARE 24, 28 (2004), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564302/pdf/bh0104024.pdf>.

59. FDA, *supra* note 42.

from exposure to light and typically require refrigeration to maintain potency.⁶⁰ These storage safety requirements pose problems for biologics manufactured on one continent and transported to another.

For example, in 2014, Ozkan Semizoglu, a Turkish drug wholesaler, was sentenced to 27 months in prison for smuggling counterfeit, misbranded, and adulterated cancer treatment drugs to the U.S.⁶¹ Semizoglu shipped biologic cancer treatments requiring cold storage without any temperature controls from Turkey to the state of Missouri.⁶² The exporter was aware the medications would arrive in the U.S. without the constant cold temperature range needed to maintain drug quality and stability.⁶³ Even legitimate drugs shipped under these conditions would not be effective treatments after such a journey heightening the risk to sick patients.

Biologic counterfeits are a concern spanning the globe. The following are just some of the examples of biologic counterfeiting incidents:

- In 2004, Florida authorities arrested suspects selling pharmaceutical counterfeits including diluted Procrit and Epogen, biologics used to boost immune systems in cancer and AIDS patients.⁶⁴ The suspects made millions in illegal profits using the illicit proceeds to purchase a strip club.⁶⁵ They continued selling phony medications out of the strip club, storing the sham medicine in beer coolers.⁶⁶
- In 2006, Brazil's pharmaceutical regulator recalled counterfeit flu vaccines marked with the brand name Fluarix.⁶⁷ The manufacturer responsible for the genuine Fluarix biologic stopped marketing the vaccine under that name two years earlier.⁶⁸ The discovery came just as a nationwide campaign to inoculate 18 million Brazilians began.⁶⁹

60. *Id.*

61. Press Release, U.S. Dept. of Justice, *Turkish Man Sentenced for Smuggling Counterfeit Cancer Drugs* (June 18, 2014), <http://www.fda.gov/ICECI/CriminalInvestigations/ucm420869.htm>.

62. *Id.*

63. *Id.*

64. Bob LaMendola, *2 Charged in Phony Drug Scheme*, SUN SENTINEL (May 28, 2004), http://articles.sun-sentinel.com/2004-05-28/news/0405280185_1_strip-club-cancer-drugs-club-employees.

65. *Id.*

66. *Id.*

67. Kubic, *supra* note 38.

68. *Id.*

69. *Id.*

- In 2011 and 2012, Chinese authorities carried out raids and made arrests when an organized crime group delivered counterfeit and diverted human growth hormone (HGH) products to local subcontractors.⁷⁰

IV. PARALLEL IMPORTING

Parallel importing is the practice of purchasing and importing legitimate goods not intended for use in a regional market, usually at a substantial price discount.⁷¹ Manufactured abroad, the imported goods bear a genuine trademark.⁷² Importers of unauthorized goods mistakenly believe that the gray market of parallel importation is a legitimate business.⁷³ However, the unauthorized flow of goods jeopardizes quality standards and projects a false sense of security in consumers.⁷⁴

Legitimate pharmaceuticals licensed for use in other countries are not approved for sale in the U.S. by parallel importing.⁷⁵ Even if the Avastin counterfeits were genuine medications, the goods are illegal in the U.S. because they were not made in approved facilities or packaged with FDA approved labeling.⁷⁶ No new drug may enter the U.S. market, by new drug approval or importation, without FDA approval of both safety and effectiveness.⁷⁷ The Food, Drug, and Cosmetics Act (FDCA) prohibits importation of unapproved drugs.⁷⁸ Unapproved drugs are medications, including foreign-made versions of U.S. approved drugs not manufactured in accordance with and pursuant to FDA approval.⁷⁹

High drug prices in the U.S. create the opportunity for parallel importers to take advantage of price discrepancies between the U.S. and other nations.⁸⁰ Parallel importation of pharmaceuticals between countries with highly developed regulatory systems trade on established goodwill and

70. INTERPOL, *supra* note 8, at 9.

71. Frances P. Hadfield, *Who's on the Hook? (and Who Can Afford the Hook Anyway?): Responding to Customs and Border Protection's Requests for Factual Information: Responsibilities, Burdens, and Consequences*, 23 TUL. J. INT'L & COMP. L. 331, 345 (2015).

72. *Id.* at 344.

73. *Id.* at 345.

74. *Id.*

75. Federal Food, Drug, and Cosmetic Act (FDCA) 21 U.S.C. § 331 (2015).

76. Benoît Faucon & Jeanne Whalen, *Fake Avastin Took Murky Path to U.S.*, WALL ST. J. (Apr. 5, 2012, 8:31 AM), <http://www.wsj.com/articles/SB10001424052702303302504577323500453577094>.

77. See NIELSON, *infra* note 157, at 28.

78. 21 U.S.C. § 331 et seq. (2015).

79. *Id.*

80. Lucy J. Minehan, *The Gray Market: A Call for Greater Protection of Consumers and Trademark Owners*, 12 U. PA. J. INT'L. BUS. L. 457, 457 (1991).

quality of reputation.⁸¹ However, public policy prohibits parallel importing from nations with weak regulatory standards. This is because drugs sold abroad may be subject to less stringent regulation and testing, posing health risks if not properly assessed in a rigorous regulatory environment.⁸²

Addressing public health inequity in trade practices, the World Trade Organization (WTO) administered the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).⁸³ The TRIPS Agreement contains provisions ensuring public health needs are addressed through international trade.⁸⁴ Parallel importing cannot be challenged and is effectively a matter of national discretion.⁸⁵ TRIPS “does not and should not prevent Members from taking measures to protect public health.”⁸⁶ This emphasizes a nation’s ability to utilize compulsory licensing and parallel importation of legitimate drugs.⁸⁷ International trade agreements often limit the flexibilities provided for by TRIPS in the name of public health.⁸⁸ Both the E.U. and U.S. limit the scope of parallel importation.⁸⁹

Limitations on pharmaceutical parallel importing are an attempt to prevent weak spots from compromising the supply chain. While some encourage gray market purchasing to keep costs down, as Minnesota did when implementing the ConnectRx program, the unique hazards associated with biopharmaceuticals highlight the need for further scrutiny.

81. *Id.* at 458.

82. *See* Summit Tech. v. High-Line Med. Instruments, 922 F. Supp. 918, 936–37 (C.D. Cal. 1996).

83. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 108 Stat. 4809, 1869 U.N.T.S. 299.

84. *See* MDG GAP TASK FORCE, MILLENNIUM DEVELOPMENT GOAL 8: THE GLOBAL PARTNERSHIP FOR DEVELOPMENT: MAKING RHETORIC A REALITY, at xvi, U.N. Sales No. E.12.II.C.5 (2012).

85. WORLD TRADE ORG. [WTO], FACT SHEET: TRIPS AND PHARMACEUTICAL PATENTS OBLIGATIONS AND EXCEPTIONS (2006), http://www.wto.org/english/tratop_e/trips_e/factsheet_pharm02_e.htm.

86. Roma Patel, *A Public Health Imperative: The Need for Meaningful Change in the Trans-Pacific Partnerships Intellectual Property Chapter*, 16 MINN. J. L. SCI. & TECH. 477, 488 (2015).

87. *Id.*

88. *Id.* at 488–89.

89. MÉDECINS SANS FRONTIÈRES, *TRIPS, TRIPS Plus and Doha* (last updated Jul. 2011), <http://www.msfaccess.org/content/trips-trips-plus-and-doha>.

V. THE AVASTIN CASE: HOW BIOLOGIC COUNTERFEITS INFILTRATED DOCTORS' OFFICES

“The Avastin case was a watershed moment for law enforcement to recognize that this is not a problem that can be restricted to one part of the world,” said Ronald Noble, Secretary-General of the international police organization INTERPOL.⁹⁰ Avastin is a life-saving cancer treatment also known as Altuzan, the product’s Turkish name.⁹¹ First approved in 2004, Avastin was developed by Genentech, an American subsidiary of Roche, to treat metastatic cancers.⁹² The injectable biopharmaceutical is a monoclonal antibody, which inhibits blood vessel forming growth factors, effectively choking off blood supply to tumors.⁹³ Avastin is on the WHO’s list of Essential Medicines, indicating its importance to public health.⁹⁴

In early 2012, the FDA warned 20 U.S. medical practices that they may have obtained counterfeit versions of Avastin. This was the first discovery in the U.S. of a counterfeit cancer drug administered in physicians’ offices.⁹⁵ The fake injectable contained cornstarch, acetone, and other chemicals, but no cancer-fighting ingredients.⁹⁶ By the end of the investigation, the FDA sent almost 1,000 warning letters to 48 states warning of the dangerous counterfeit.⁹⁷

The Avastin counterfeits took a long, international route to the United States. The fake drugs originated in Turkey and were exported by Ozay Pharmaceuticals (Ozay), which shipped supplies to over 70 countries.⁹⁸ Sometimes, the fake Avastin shipped directly from Turkey to the United States.⁹⁹ Other times, the counterfeit pharmaceuticals took a circuitous route,

90. Weaver, *supra* note 18.

91. *Id.*

92. Genentech, Product Information (last visited Dec. 22, 2016), <https://www.genec.com/media/product-information/avastin-colorectal>.

93. See FEDERAL FOOD AND DRUG ADMIN. [FDA], *FDA News Release* (Feb. 26, 2004), <http://www.fda.gov/newsevents/newsroom/pressannouncements/2004/ucm108252.htm>.

94. WORLD HEALTH ORG. [WHO], WHO MODEL LIST OF ESSENTIAL MEDICINES 42 (2015), http://www.who.int/selection_medicines/committees/expert/20/EML_2015_FINAL_amended_AUG2015.pdf?ua=1.

95. Weaver, *supra* note 18.

96. *See id.*

97. See Tim K. Mackey et al., *After counterfeit Avastin®—what have we learned and what can be done?*, 12 NATURE REVS. CLINICAL ONCOLOGY 302, 302 (2015), <http://www.nature.com/nrclinonc/journal/v12/n5/abs/nrclinonc.2015.35.html>.

98. See Lecia Bushak, *Turkish Man, Owner Of Ozay Pharmaceuticals Admits To Importing Illegal Cancer Drugs Into US*, MEDICAL DAILY (Aug. 16, 2014, 4:55 PM), <http://www.medicaldaily.com/turkish-man-owner-ozay-pharmaceuticals-admits-importing-illegal-cancer-drugs-us-298366>.

99. See Jeanne Whalen, *Turkish Drug Exporter Ozay Draws U.S. Scrutiny*, WALL ST. J. (Apr. 7, 2014, 7:46 PM), <http://www.wsj.com/articles/SB10001424052702303546204579435692215579758> (noting that Sabahaddin Akman, owner of Ozay Pharmaceuticals

shipping from Ozay to River East Supplies in the United Kingdom,¹⁰⁰ then to Canada Drugs in Canada, and then finally to Montana Healthcare Solutions in the United States.¹⁰¹ While Ozay sometimes sent legitimate drugs unlicensed for use in the U.S., other times it shipped complete fakes containing water and mold.¹⁰² Ozay also sent biologic shipments without proper protections to keep the sensitive drugs at a constant cold temperature required for drug stability.¹⁰³ The company also mislabeled shipments calling them “gifts” or “product samples” to avoid detection by customs officials.¹⁰⁴ These parallel import transgressions undermine safety regulations intended to protect patients.

By 2011, U.S. doctors could no longer make a living purchasing the drug from legitimate U.S. suppliers due to Medicare and insurance companies reducing payments.¹⁰⁵ A vial of Avastin cost about \$2,400,¹⁰⁶ a year’s worth of treatment could exceed \$100,000.¹⁰⁷ Doctors began purchasing counterfeit Avastin from U.S. drug wholesaler Montana Healthcare Solutions at deep discounts.¹⁰⁸ Ironically, Minnesota reacted to high drug prices in 2004 by connecting residents with state-approved foreign pharmacies through the Minnesota RXConnect online drug importation program.¹⁰⁹ Minnesota inspected and approved pharmacies despite warnings from the FDA about

pled guilty to importing counterfeit drugs into the U.S. after a sting in Puerto Rico, and numerous agencies were involved in the apprehension; Akman claimed the drug shipments were gifts to avoid raising suspicion by customs officials).

100. *See id.*; *see also* Weaver, *supra* note 18.

101. *See* Weaver, *supra* note 18.

102. *See* Jeanne Whalen, *Arrests in Cancer Drug Sales*, WALL ST. J. (Feb. 14, 2014, 6:26 PM), <http://www.wsj.com/articles/SB10001424052702304703804579383271726960510>.

103. *See* S. Imber, *Man Imported Fake Cancer Drugs From Turkey Gets 2 Years and 3 Months in Prison*, PARTNERSHIP FOR SAFE MEDICINES (Nov. 4, 2014), <http://www.safe-medicines.org/2014/11/man-imported-fake-cancer-drugs-from-turkey-gets-2-years-and-3-months-in-prison-11-4-14.html> (providing graphic for regional scope of indictments and guilty verdicts).

104. *See id.*

105. *See* Weaver, *supra* note 18.

106. *Id.*

107. A. Jirillo, F. Vascon & M. Giacobbo, *Bevacizumab in advanced cancer, too much or too little?*, 19 ANNALS OF ONCOLOGY 1817, 1817 (2008), <http://annonc.oxfordjournals.org/content/19/10/1817.full>.

108. *See* Weaver, *supra* note 18.

109. Kevin Goodno & Karen Janisch, *Minnesota: Leading the Way on Canadian Prescription Medicine Importation*, 31 WM. MITCHELL L. REV. 811, 814 (2005).

the risk.¹¹⁰ For example, Minnesota added Canada Drugs, a suspect supplier discussed below, to the approved list¹¹¹ even though representatives from other states had concerns.¹¹² The RXConnect program eventually ended in 2010.¹¹³

Montana Healthcare Solutions was one of many subsidiaries controlled by Mr. Kris Thorkelson.¹¹⁴ Also known by other names, Montana Healthcare Solutions was part of the supply chain consisting of a maze of subsidiaries importing medicines from the international gray market controlled by Mr. Thorkelson to obfuscate the origin of drug shipments.¹¹⁵ Founding pharmaceutical distributor Canada Drugs in 2001, the company at first sold medications obtained solely from Canadian suppliers; however, within a decade it began importing drugs from questionable sources.¹¹⁶

The fake Avastin was likely manufactured in Turkey and traveled through Europe before importation into Canada, where it was sold to doctors in the U.S.¹¹⁷ In 2012, Montana Health Solutions, which sold the fake Avastin to U.S. doctors, procured the drug through a company founded by Mr. Thorkelson's brother-in-law known as River East Supplies, a U.K. wholesaler obtaining cheap medications from locations such as India and Turkey.¹¹⁸ The wholesaler from Turkey was not registered with Turkish authorities as a pharmaceutical exporter as required by law.¹¹⁹ Investigations later revealed that there was no pharmaceutical exporter at the Turkish address on the invoices; rather, the location was home to a textiles factory.¹²⁰

110. Helkei Tinsley, *Current Public Law and Policy Issues: Prescriptions without Borders: America Looks to Canada for Answers to Solve the Prescription Drug Pricing Predicament in the U.S., but is Importation Really the Solution?*, 25 *HAMLIN J. PUB. L. & POL'Y* 437, 465, 470–71 (2004).

111. *Two Pharmacies Added to Minnesota RxConnect Web Site*, *CAPITOL REP.* (June 21, 2004), <http://politicsinminnesota.com/2004/06/two-pharmacies-added-to-minnesota-rxconnect-web-site/>; see also Fred Schneyer, *MN Starting Canadian Pharmacy Inspections*, *PLAN SPONSOR* (Mar. 5, 2004), <http://www.plansponsor.com/MN-Starting-Canadian-Pharmacy-Inspections/>.

112. John M. Taylor, III, Associate Comm'r for Regulatory Affairs, Food & Drug Admin., Address Before the Permanent Subcomm. on Investigations: Importation of Prescription Drugs (July 22, 2004), <http://www.fda.gov/NewsEvents/Testimony/ucm113635.htm>.

113. *Minnesota ends prescription importation program*, *AM. MED. NEWS* (Jan. 29, 2010), <http://www.amednews.com/article/20100129/business/301299997/8/>.

114. See Weaver, *supra* note 18.

115. *Id.*

116. *Id.*

117. See *id.*

118. *Id.*

119. Faucon, *supra* note 76.

120. *Id.*

A second wave of fake Avastin later entered the U.S. in spite of ongoing investigations.¹²¹ In this case, the counterfeits likely originated in Egypt.¹²² Once again, River East Supplies, the U.K. wholesaler that imported the initial batches of counterfeit Avastin, continued importing more fake medication.¹²³

Another faulty link in the supply chain, Richard's Pharma, a licensed U.K. wholesaler, originally procured the counterfeit medicine from a Turkish wholesaler, exporting nearly a third of the counterfeit inventory directly to the United States.¹²⁴ The remaining counterfeits were sold to River East Supplies, which also imported the fakes to the United States.¹²⁵ A director at River East Supplies said the company only buys drugs from "regulated supply channels and through licensed wholesalers."¹²⁶ Hazardous counterfeits crossed borders without repercussion even though the companies were already on alert from the previous counterfeiting incident.

At least 76 doctors in 22 states purchased the counterfeit Avastin.¹²⁷ The drugs came through many suppliers and distributors affiliated with Canada Drugs.¹²⁸ The genuine manufacturer and U.S. government responded with public education campaigns, including publishing identification tips on the Internet.¹²⁹ The counterfeits were easily identifiable due to inconsistencies in the packaging, which readily indicated a lack of approval in the United States.¹³⁰

A California physician who received the counterfeits said that he was unaware the drugs were not FDA-approved because the suppliers had valid wholesaler licenses from U.S. state regulators.¹³¹ When customers expressed concerns to Canada Drugs that the medication originated in Turkey, they were told that "every country has a standard they have to pass and some of those countries have stricter standards than the U.S."¹³²

121. *See id.*

122. *Id.*

123. *Id.*

124. *See id.*

125. *Id.*

126. *Id.*

127. *See Weaver, supra* note 18.

128. *Id.*

129. *See Genentech Statement on Counterfeit Drug Labeled as Altuzan (Bevacizumab) in the United States*, GENENTECH (Feb. 11, 2013), http://www.gene.com/media/statements/ps_020713.

130. *Id.*

131. *See Weaver, supra* note 18.

132. *Id.* In a related incident, a Swiss distributor ordered what it thought to be the genuine drug from an Egyptian company called Sawa, a company unregistered with Egypt's

While pharmaceutical wholesalers are not in a position to perform testing for purity and strength by analytical standards, they can take reasonable precautions to verify that shipments are legitimate. Reasonable precautions include examining the packaging for inconsistencies, such as multiple languages, and ensuring use of appropriate cold storage during transport. These basic precautions can be utilized by a simple inspection when shipments are received. However, in spite of the heightened risk of importing from countries with lax regulatory schemes, and in the face of inconsistent product packaging, the counterfeits went undetected until reaching doctors' offices in the United States.

The U.S. government prosecuted both doctors and importers responsible for the fake Avastin supplies. The owner of Montana Health Solutions, Mr. Paul Bottomley, was sentenced to house arrest and five years of probation.¹³³ He forfeited millions in assets and was ordered to perform 200 hours of community service.¹³⁴ The owner of Richard's Pharma, Mr. Richard Taylor, was sentenced to 18 months in prison.¹³⁵ None of the prosecutions, however, included charges for injury or harm to patients that were relying on receiving genuine, life-saving medicine.¹³⁶ The lost opportunity for sick people to receive treatment in a critical moment could literally be a death sentence for them, but with no repercussions to those who failed to supply the necessary treatment.

While sick patients may miss opportunities for recovery when given ineffective drugs, counterfeit Avastin has also been found to contain harmful bacteria.¹³⁷ Over 100 people were given contaminated counterfeits in China in 2010 in ocular treatments.¹³⁸ Over half of the patients suffered from serious eye inflammation after receiving the dangerous counterfeit during off-label use.¹³⁹ Fortunately, the ophthalmology patients recovered with appropriate

health ministry. The counterfeit drugs passed from Egypt, to Switzerland, to Denmark, and the U.K. prior to discovery in the U.S. Contacts at Sawa claimed the Egyptian company obtained the drugs from Turkey. Swiss law required pharmaceutical wholesalers to "ensure the pharmaceutical quality" of the products. *See* Faucon, *supra* note 76.

133. *See* Mackey, *supra* note 97, at 308, tbl. 1.

134. *Id.*

135. *Id.*

136. *See id.*

137. S. Imber, *Fake Cancer Drug Ring Exposed in Chinese Trial*, PARTNERSHIP FOR SAFE MEDS. (May 20, 2011), <http://www.safemedicines.org/2011/05/fake-cancer-drug-ring-exposed-in-chinese-trial-253.html>.

138. *Id.*

139. S. Imber, *Thirteen Indicted of Infiltrating Hospital with Fake Drugs*, PARTNERSHIP FOR SAFE MEDS. (Apr. 26, 2011), <http://www.safemedicines.org/2011/04/thirteen-indicted-of-infiltrating-hospitals-with-fake-drugs-225.html>.

treatment.¹⁴⁰ Increasing sentencing guidelines and penalties not only provides deterrence, but also is more fair in relation to the severity and potential to profit off the crime.

CanadaDrugs, which sold the Avastin counterfeits, continues to operate today.¹⁴¹ The website continues to market to U.S. consumers and purports to receive medication from reputable sources.¹⁴² Indictments against CanadaDrugs, its subsidiaries, and its employees also continue.¹⁴³ Allegations of bribery, smuggling, and the cover-up endure against the company and the entities that certified it to bring a “vener of legitimacy.”¹⁴⁴

VI. INTERNATIONAL SUPPLY CHAIN CONCERNS

The Avastin case exposed loopholes in a previously robust supply chain. The drive for cheaper prices and increasing number of links in the supply chain weakened quality protections. Each nation in the supply chain had standards for pharmaceutical import and export. An examination of those standards and the agencies charged with enforcement will show the landscape in which counterfeits can be introduced to each market.

A. United States

In 2013, the U.S. accounted for 41% of the global pharmaceutical market.¹⁴⁵ The U.S. is also a global leader in pharmaceutical research and development, spending approximately \$40 billion annually.¹⁴⁶ The U.S. has typically

140. See Xiaodong Sun, M.D., Xun Xu, M.D., & Xi Zhang, M.D., *Counterfeit Bevacizumab and Endophthalmitis*, NEW ENG. J. MED. 378, 378–79 (2011), <http://www.nejm.org/doi/full/10.1056/NEJMc1106415>.

141. See CANADADRUGS, <https://www.canadadrugs.com/>.

142. See *id.*

143. See U.S. v. CanadaDrugs.com, No. CR14-27-BU-DLC, (Mont., July 17, 2015) (United States Courts Archive); see also Matt Voltz, *U.S. Charges Canadian Company with Smuggling, Money Laundering*, FLATHEAD BEACON (Aug. 10, 2015), flatheadbeacon.com/2015/08/10/u-s-charges-canadian-company-with-smuggling-money-laundering/.

144. John Horton, *CanadaDrugs.com Indictment Exposes Fake Drug Sales, Pharmacy Checker Role*, LEGIT SCRIPT (Aug. 18, 2015), <https://blog.legitscript.com/2015/08/canada-drugs-com-indictment-exposes-fake-drug-sales-pharmacychecker-role/>.

145. EFPIA, *supra* note 46, at 5.

146. *Id.*

experienced low rates of pharmaceutical counterfeits in the marketplace.¹⁴⁷ It is also a leader in introducing biologicals.¹⁴⁸

The FDA has the regulatory authority to approve drugs.¹⁴⁹ In the U.S., pharmaceuticals are labeled following stringent guidelines from the FDA.¹⁵⁰ When the FDA reviews an application for a new drug, it considers what information should appear on the drug's label.¹⁵¹ The labeling must only include uses supported by substantial evidence of safety and effectiveness.¹⁵² Drug labels must provide all medically relevant information for appropriate use of the product including dosage, directions for administration, precautions, warnings, and contradictions.¹⁵³

Furthermore, the U.S. has extensive and detailed regulations regarding Good Manufacturing Practices (GMP) in the manufacture of pharmaceuticals.¹⁵⁴ GMP regulations are the minimum requirements for drug manufacturing, processing, and packaging that ensure drug products are safe, with the ingredients and dosage strength that the labeling claims.¹⁵⁵ Drugs not manufactured under GMP standards are presumed adulterated under the FDCA.¹⁵⁶ This is due to the risk to public health from impure drugs, which is greater than the financial hardship and inconvenience suffered by a manufacturer who produces medication without the appropriate controls.¹⁵⁷

The Office of Criminal Investigations (OCI), a division of the FDA, is responsible for investigating criminal violations of FDA-regulated products.¹⁵⁸

147. IMPACT, *supra* note 2, at 1.

148. Pharmaceutical Research and Manufacturers of America, *2013 Biopharmaceutical Research Industry Profile*, PHARMA 20 (July 2013), <http://www.phrma.org/sites/default/files/pdf/PhRMA%20Profile%202013.pdf>.

149. See U.S. FOOD & DRUG ADMIN. [FDA], *Development & Approval Process (Drugs)* (last accessed Nov. 25, 2016), <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/>; see also NIELSON, *supra* note 157, at 27.

150. See FDA, *Labeling* (last updated Aug. 27, 2015), <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm065010.htm>.

151. See Jeffery N. Gibbs, *Food & Drug Administration Regulation & Products Liability: Strong Sword, Weak Shield*, 22 TORT & INS. L.J. 194, 211 (1987).

152. See *id.*

153. See 21 C.F.R. § 201.56(d)(1) (2016).

154. 21 C.F.R. § 211.1 et seq. (2016).

155. See FDA, *Drug Applications and Current Good Manufacturing Practice (CGMP) Regulations*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm090016.htm>.

156. See FDA, *Facts About the Current Good Manufacturing Practices (CGMPs)*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm169105.htm>.

157. See JAMES ROBERT NIELSON, *HANDBOOK OF FEDERAL DRUG LAW* 15 (1992).

158. See FDA, *Inspections, Compliance, Enforcement, and Criminal Investigations*, <http://www.fda.gov/ICECI/CriminalInvestigations/ucm123027.htm> ("All reports of counterfeiting, tampering or tampering threats must be immediately reported to the Office of Criminal Investigations (OCI) Headquarters' Office, SAIC-IOD (Special Agent in Charge- Investigative

The FDA also works with Customs and Border Patrol (CBP) to enforce importation violations.¹⁵⁹ Even if a counterfeit drug is detained, its sponsor can apply to have the drug returned within 90 days, which often leads to counterfeiters repackaging and reshipping the drugs back to the United States.¹⁶⁰

B. Canada

Health and Welfare Canada is the federal Canadian department responsible for “promoting and preserving the health, safety and well-being of all Canadians.”¹⁶¹ The Health Protection Branch (HPB) of Health and Welfare Canada oversees the “availability, use, manufacture and sale” of pharmaceuticals.¹⁶² The HPB evaluates new drug submissions, analyzes health hazards, and inspects manufacturing plants.¹⁶³ The HPB is authorized to bring criminal charges for non-compliance with Canadian laws and regulations.¹⁶⁴

Canada pharmaceutical policy favors affordability.¹⁶⁵ Pharmaceutical sales in Canada are 2.5% of the global market.¹⁶⁶ Drug prices in Canada are lower than the U.S. due to drug reference pricing implemented by Canada’s Patent Act.¹⁶⁷ The Patent Act established the Patented Medicine Prices Review Board (PMPRB) in response to high drug prices in Canada.¹⁶⁸ The

Operations Division) (301-276-9500) and the Office of Crisis Management (OCM)/Office of Emergency Operations (OEO), HFA-615, (301-796-8240).”).

159. COUNTERFEIT PHARMACEUTICAL INTER-AGENCY WORKING GROUP, REPORT TO THE VICE PRESIDENT OF THE UNITED STATES AND TO CONGRESS 2 (2011), https://www.whitehouse.gov/sites/default/files/omb/IPEC/Pharma_Report_Final.pdf.

160. PHARMACEUTICAL MANUFACTURING, *FDA Finalized Authority to Destroy Rejected Drug Imports* (Sept. 15, 2015), <http://www.pharmamanufacturing.com/industrynews/2015/fda-finalizes-authority-destroy-rejected-drug-imports/>.

161. EILEEN MCMAHON, NEW DRUG APPROVAL IN CANADA 80 (1995).

162. HEALTH PROTECTION BRANCH [HPB], HEALTH PROTECTION & DRUG LAWS 9 (1991).

163. *Id.* at 11–12.

164. Patricia I. Carter, *Federal Regulation of Pharmaceuticals in the United States and Canada*, 21 LOY. L.A. INT’L & COMP. L.J. 215, 224 (1999).

165. Aslam H. Anis, *Pharmaceutical policies in Canada: Another Example of Federal–Provincial Discord*, 162 CANADIAN MED. ASS’N J. 523, 525 (2000), <http://www.cmaj.ca/content/162/4/523.full.pdf>.

166. INVEST IN CANADA, *Biopharmaceuticals 2* (2014), <http://www.international.gc.ca/investors-investisseurs/assets/pdfs/download/canada-biopharmaceuticals-2014.pdf>.

167. Patented Medicines Regulations (Patent Act), S.O.R. 94-688 (Can.).

168. *See generally* Carter, *supra* note 164, at 245. *See* An Act to Amend the Patent Act, 1987 S.C. c. 41.

PMPRB is an independent, quasi-judicial body with the authority to investigate and regulate excessive pharmaceutical pricing.¹⁶⁹ Determination of excessive prices is based on a comparison between Canadian prices and the prices in other markets, the prices of similar medications in Canada, and changes in Canada's Consumer Price Index.¹⁷⁰ Lower prices in Canada attract customers from America where there are no drug price controls.¹⁷¹

All pharmaceuticals imported into Canada must meet the standards and regulations of the Food and Drug Act.¹⁷² Canadian labeling guidelines require a drug's label to contain only the name of the drug, adequate direction for use, a quantitative list of active ingredients, expiration date, potency, and method of administration.¹⁷³ Canada also adopts GMP requirements for pharmaceutical manufacturing.¹⁷⁴

While the GMP requirements of the U.S. and Canada are similar, Canada has not adopted the policy of presuming pharmaceuticals are adulterated if Canadian GMP standards are not met.¹⁷⁵ Canadian law explicitly prohibits selling misleading or deceptive drugs.¹⁷⁶ The HPB issues Drug Identification Number (DIN) to pharmaceuticals.¹⁷⁷ The DIN system provides information regarding the drug's manufacture, use, effects, and ingredients.¹⁷⁸

C. European Union

Counterfeit drugs accounted for nearly a quarter of all counterfeit goods seized in the European Union in 2011.¹⁷⁹ The E.U. does not have a harmonized system for setting pharmaceutical quality and safety standards.¹⁸⁰ Member nations are currently responsible for setting their own standards.¹⁸¹ The

169. See Canadian Centre on Substance Abuse Act, R.S.C. 1985, c. L-49.

170. R.S.C. 1985, c. P-4 § 85(1) (Can.).

171. Lana Kraus, *Note: Medication Misadventures: The Interaction of International Reference Pricing and Parallel Trade in the Pharmaceutical Industry*, 37 *VAND. J. TRANSNAT'L L.* 527, 538 (2004).

172. See Food and Drugs Act, R.S.C. 1985, c. F-27 (Can.).

173. McMAHON, *supra* note 161, at 80.

174. See Food and Drugs Act, R.S.C. 1997, c. F-27, §§ 21.2-21.3 (Can.).

175. Carter, *supra* note 164, at 240.

176. Food and Drugs Act, R.S.C. 1985, c. F-27, § 9(1) (Can.).

177. See Food and Drug Regulations, C.R.C., c. 870, § C.01.014.1(1) (Can.). See generally HPB, *supra* note 162, at 27.

178. See Food and Drug Regulations, C.R.C., c. 870, §§ C.01.014.1(2)-(3) (Can.).

179. John Lechleiter, *Exposing and Eradicating the Dark World of Fake Pharmaceuticals*, *FORBES* (Aug. 22, 2012, 12:22 PM), <http://www.forbes.com/sites/johnlechleiter/2012/08/22/exposing-and-eradicating-the-dark-world-of-fake-pharmaceuticals/>.

180. See *Norms, Standards, and Guidance for Pharmaceuticals*, WORLD HEALTH ORG. [WHO], http://www.who.int/medicines/areas/quality/safety/quality_assurance/norms_standards/en/ (last visited Nov. 29, 2016).

181. See Comm'n Delegated Regulation (EU) No. 1252/2014 of 28 May 2014 supplementing Directive 2001/83, of the European Parliament and of the Council with

E.U. has, however, addressed counterfeiting in the Falsified Medicines Directive.¹⁸² As part of the international supply chain, members of the E.U. have obligations to take necessary measures to prevent pharmaceuticals introduced into the E.U., but not intended for commercialization in the E.U., from entering circulation if there are sufficient grounds to suspect falsification.¹⁸³ However, there are no concrete, established guidelines for members to follow when assessing the potential falsified character of those products.¹⁸⁴ Despite being a transient stop on the counterfeit Avastin's importation route, this obligation did not stop the fake biologic from passing through E.U.'s borders.

The E.U. has adopted legislative proposals for pharmaceutical quality.¹⁸⁵ In particular, the aim is to address the risk of falsified medicines entering the legal supply chain.¹⁸⁶ The proposals introduce unique identifiers to facilitate the verification of pharmaceutical authenticity.¹⁸⁷ Regulations for verifying drug identity were promulgated in 2016 detailing safety features such as scannable barcodes and information harmonization among nations.¹⁸⁸

The current lack of standardization across the E.U. is a regulatory point of weakness where counterfeits originating outside of the E.U. may entrench themselves in the supply chain due to confusion of requirements. The perception of the E.U. having a strong quality system leads to greater trust in parallel imports, even where heightened risks exist.

regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use, 2014 O.J. (L 337) 1 (EU).

182. See Directive 2011/62, of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human Use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, 2011 O.J. (L 174) 74 (EU).

183. *Id.*

184. See *Falsified Medicines*, EUROPEAN COMMISSION, http://ec.europa.eu/health/human-use/falsified_medicines/index_en.htm (last visited Feb. 4, 2016) [hereinafter *Falsified Medicines*].

185. See Directive 2001/83, of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, 2001 O.J. (L 311) 67 (EC).

186. See *Falsified Medicines*, *supra* note 184.

187. See Directive 2011/62, *supra* note 182.

188. Commission Regulation 2016/161, 2016 O.J. (L 32) 1 (EU).

D. Turkey

The Turkish Pharmaceutical and Medical Device Institution (Institution) regulates pharmaceuticals.¹⁸⁹ The Institution is responsible for imports, exports, licensing, manufacturing, and general control of pharmaceuticals.¹⁹⁰ In Turkey, the Pharmaceutical and Medical Preparation Law govern medications.¹⁹¹ There are also three industry-based associations establishing guidelines in Turkey and each has their own code of practices.¹⁹² The Turkish regulatory framework includes granting marketing authorizations,¹⁹³ labeling specifications,¹⁹⁴ and monitoring requirements.¹⁹⁵

The Turkish Pharmacists' Association regulates Turkish pharmaceutical imports.¹⁹⁶ The Association only allows products registered in their system to be imported.¹⁹⁷ The system includes information regarding the product names that may be imported, including the source of the product.¹⁹⁸

There is no specific law or regulation targeting counterfeiting and illegal distribution of medications in Turkey.¹⁹⁹ A counterfeiter causing "risk to another's life and health" is punishable with one to five years of imprisonment and a punitive fine.²⁰⁰ The punishment increases if a person acting within the scope of their profession commits the offense.²⁰¹ Misuse of a trademark

189. Özge Atılğan Karakulak et al., *Turkey*, in GETTING THE DEAL THROUGH, LIFE SCIENCES 2016 1 (Alexander Ehlers ed. 2016); Decree Law No. 663, 2011 (Turk.).

190. Karakulak, *supra* note 189.

191. *Id.*; Decree Law No. 1262, 1928 (Turk.); *see also* Baris Kalayci, Hande Hançer & Pinar Arıkan, *Turkey: Selection, Clearance, and Registration*, WORLD TRADEMARK REV. (last visited Feb. 7, 2016), <http://www.worldtrademarkreview.com/Intelligence/Pharmaceutical-Trademarks/2015/Country-chapters/Turkey>.

192. Karakulak, *supra* note 189, at 119 (the Turkey Pharmaceutical Industry Association (TISD), the Association of Research-Based Pharmaceutical Companies (AIFD), and the Pharmaceuticals Manufacturers Association (IEIS)).

193. *See* Licensing of Medicinal Products for Human Use (Licensing Regulation) (Official Gazette No. 25705 of 19 Jan. 2005) (Turk.); Özge Atılğan Karakulak & Tuğçe Avcısirt Geçgil, *Distribution and Marketing of Drugs in Turkey: Overview*, PRACTICAL LAW (Sept. 1, 2015), <http://us.practicallaw.com/2-618-7255> [hereinafter *Distribution and Marketing of Drugs in Turkey*].

194. Regulation on Labeling and Packaging of Medicinal Products for Human Use (Labeling Regulation) (Official Gazette No. 25904 of 12 August 2005) (Turk.); *Distribution and Marketing of Drugs in Turkey*, *supra* note 193.

195. Regulation on Safety Monitoring of Medicinal Products for Human Use (Safety Regulation) (Official Gazette No. 28973 of 15 April 2014) (Turk.); *Distribution and Marketing of Drugs in Turkey*, *supra* note 193.

196. Karakulak, *supra* note 189, at 122.

197. *Distribution and Marketing of Drugs in Turkey*, *supra* note 193.

198. Karakulak, *supra* note 189, at 122 (explaining the Pharmaceutical Importation Programme).

199. *Id.* at 123.

200. *Id.*; Turk. Crim. C. art. 186.

201. Karakulak, *supra* note 189, at 12; Turk. Crim. C. art. 186.

is also punishable.²⁰² If counterfeit medicines are imported into Turkey without being subject to customs procedures, the products will be subject to smuggling penalties as well.²⁰³

License and marketing authorization is continuously under the scrutiny of a qualified physician responsible for pharmacovigilance.²⁰⁴ The Turkish Pharmacovigilance Centre (TUFAM) is the competent authority to follow the pharmacovigilance reports and constantly updates the database.²⁰⁵ Pharmaceuticals cannot be marketed in Turkey unless properly licensed.²⁰⁶

VII. PUBLIC POLICY AND RESPONSE

“We’re seeing a lot of places that are reporting to the wrong agencies . . .” said Gaurvika Nayyar, a programme manager with the US Pharmacopeial Convention, a nonprofit which sets standards for drug quality.²⁰⁷ Numerous governmental agencies and working groups tasked with tracking and enforcing counterfeit laws have sprung up in response to the growing counterfeit problem.²⁰⁸ Policy response has leveraged focus on public education.²⁰⁹ International coordination by public and private sources also

202. Decree Law No. 556. Art. 61 (Turk.).

203. See Law to Counter Smuggling No. 5607 (Turk.).

204. Karakulak, *supra* note 189, at 13.

205. *Id.*

206. *Id.* (marketing authorization granted by the Ministry of Health pursuant to the Licensing Regulation).

207. Perks, *supra* note 10; see also U.S. Pharmacopeial Convention, <http://www.usp.org/about-usp> (last visited Feb. 28, 2016).

208. Many collaborative private and government groups have formed to educate the public and monitor counterfeit pharmaceutical activity. For example, the Permanent Forum on International Pharmaceutical Crime (PFIPC) is an international enforcement forum aimed at protecting public health and safety through the exchange of information and ideas to foster mutual cooperation. PERMANENT FORUM ON INTERNATIONAL PHARMACEUTICAL CRIME (last visited Feb. 7, 2016), <http://www.pfipc.org/>. The members of PFIPC are dedicated professionals from 15 countries whose goal is to enhance the protection of public health by combatting pharmaceutical crime. See PERMANENT FORUM ON INTERNATIONAL PHARMACEUTICAL CRIME (last visited Feb. 7, 2016), <http://www.pfipc.org/who-we-are>. The Heads of Medicines Agencies—Working Group of Enforcement Officers (HMA-WGEO) was established to contribute to the protection of public health and welfare, including animal health, through ensuring adherence to the regulations of manufacturing and distribution chains of medicinal products, disruption of illegal activities and the sharing of information. HEADS OF MEDICINES AGENCIES (last visited Feb. 7, 2016), <http://www.hma.eu/wgeo.html>.

209. COUNTERFEIT PHARMACEUTICAL INTER-AGENCY WORKING GROUP, *supra* note 159, at 10–13.

seeks to harmonize import and export policies introducing new advancements in technology to secure the supply chain.

A. World Health Organization

The WHO is a United Nations agency fostering international cooperation in the health field.²¹⁰ The WHO develops and promotes international standards, nomenclature, and guidelines concerning biological and pharmaceutical substances.²¹¹ The WHO adopts conventions on worldwide health matters.²¹² Conventions are binding treaties.²¹³ Regulations adopted by the WHO's Health Assembly come into force for all members unless duly rejected.²¹⁴ Regulations are binding obligations, unlike resolutions and recommendations, which are not legally binding.²¹⁵

The WHO Certification Scheme for the Quality of Pharmaceutical Products (Certification Scheme) recommends uniform guidelines for the international supply chain.²¹⁶ The WHO adopted these guiding principles for national regulatory authorities to assure not only the quality, but also the safety and efficacy, of pharmaceutical products in international commerce.²¹⁷ The Certification Scheme is a voluntary administrative agreement facilitating international pharmaceutical trade.²¹⁸

The principles, adopted in 1986, emphasize the need for a formal agreement between participating Member States to provide information on pharmaceutical exports.²¹⁹ It requires registration status in the country of origin and information concerning manufacturer compliance with the WHO's GMP guidelines.²²⁰ To maximize effectiveness, the Certification Scheme ensures that imported products are in conformity with relevant import license

210. KELLEY LEE, THE WORLD HEALTH ORGANIZATION (WHO) 1 (Thomas G. Weiss ed., 2009).

211. *Id.* at 18.

212. WHO CONST. art. 19 (1946).

213. LAWRENCE O. GOSTIN, GLOBAL HEALTH LAW 110 (2014).

214. WHO CONST. art. 21; *id.* art. 22 (1946).

215. GIAN LUCA BURCI & CLAUDE-HENRI VIGNES, WORLD HEALTH ORGANIZATION 56 (2004).

216. WORLD HEALTH ORGANIZATION, GUIDELINES ON IMPORT PROCEDURES ON PHARMACEUTICAL PRODUCTS, WHO TECHNICAL SUPPORT SERIES NO. 863, 185 (1996), http://www.who.int/medicines/areas/quality_safety/quality_assurance/GuidelinesImportProceduresPharmaceuticalProductsTRS863Annex12.pdf.

217. *Id.* at 185.

218. WORLD HEALTH ORGANIZATION [WHO], *WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce: Questions and Answers* (May 2010), http://www.who.int/medicines/areas/quality_safety/regulation_legislation/certification/qas_certif_scheme_2011.pdf.

219. WHO, *supra* note 216, at 185.

220. *Id.*

regulations.²²¹ The Certification Scheme secures the supply chain by regulating storage and transit facilities with controls at every stage of transportation.²²²

The Certification Scheme advises that importation of pharmaceuticals be implemented by national drug regulatory authorities (DRA).²²³ Accordingly, importation of pharmaceutical products would be channeled exclusively through a national customs post specifically designed for drug imports.²²⁴ Only products appropriately licensed for marketing within the importing country would be cleared through the specialized customs post.²²⁵ To facilitate legitimate importation, the customs post would have centrally compiled information concerning authorized import agents, issue notifications, and similar alerts for specialized screening of pharmaceutical imports.²²⁶ Implementation of controls is further outlined in the Certification Scheme.²²⁷

Varying levels of sophistication between nations means that there is variance in the implementation of the Quality Scheme.²²⁸ Improvements to the Quality Scheme are monitored, evaluated, and updated as the global pharmaceutical industry responds to supply chain conditions.²²⁹ The WHO has also adopted notification requirements to the Division of Drug Management and Policies.²³⁰

B. Private Action by the Pharmaceutical Industry

The pharmaceutical industry is on the front lines of the fight against counterfeits. Private drug companies drive many counterfeiter convictions.²³¹ Due to the great investments made in research and development and the additional cost of regulatory compliance, drug companies have a compelling

221. *Id.*

222. *Id.*

223. *Id.* at 186.

224. *Id.*

225. *Id.*

226. *Id.*

227. *See id.*

228. *See generally* Anna Sahl, Relevance of a Certificate of Pharmaceutical Product for Registration and Life Cycle Management of Imported Drugs (2013) (unpublished Masters thesis, Bonn University), http://dgra.de/media/pdf/studium/masterthesis/master_sahl_a.pdf.

229. *See generally id.*

230. WHO, *supra* note 216, at 189.

231. Barbara Moran, *Cracking Down on Counterfeit Drugs*, NOVA NEXT (Aug. 20, 2013), <http://www.pbs.org/wgbh/nova/next/body/uncovering-counterfeit-medicines/>.

interest in protecting the public from detrimental effects of fake pharmaceuticals.

The Pharmaceutical Research and Manufacturers of America (PhRMA) is a trade organization of biopharmaceutical researchers and biotechnology companies.²³² PhRMA members work to improve pharmacologic vigilance by forming policies that may eventually be adopted by law. In 2003, PhRMA members adopted a voluntary notification system agreeing to notify the OCI of counterfeit discoveries within five days.²³³ U.S. law now requires notification.²³⁴

Track and trace systems play a major role in the legitimate supply chain. Manufacturers use technology to control and monitor the supply chain. Radio-frequency identification (RFID) is used by manufacturers to track and trace products moving through the supply chain.²³⁵ In another technological advancement, research teams are developing 3D barcodes to authenticate products.²³⁶ Barcodes are beneficial because they are scannable by anyone with a smartphone.²³⁷ The benefits of tracking and tracing technology to both patients and manufacturers are decreases in the cost due to security and efficiency.

The pharmaceutical industry is developing other means of verifying drug identity. For example, scientists are using spectroscopy to authenticate the chemical fingerprint of biologics.²³⁸ Spectroscopy is wavelength measurement of light refraction.²³⁹ The technique is noninvasive, making direct analysis possible through packaging such as a glass vial.²⁴⁰ Another advantage is that inspectors can perform analysis using hand held scanners.²⁴¹ Direct analysis of biopharmaceuticals is an advantage when counterfeiters dilute genuine drugs or mix counterfeits into a shipment of legitimate medicines.

The pharmaceutical industry uses traditional supply chain techniques along with more sophisticated methods to ensure the supply of safe pharmaceuticals

232. PhRMA, *About PhRMA* (last visited Feb. 7, 2016), <http://www.phrma.org/about>.

233. Nelson, *supra* note 17, at 1082.

234. Drug Supply Chain Security Act (DSCSA), § 582(b)(4)(B) (2012).

235. See *Product Counterfeiting: How Fakes are Undermining U.S. Jobs, Innovation, and Consumer Safety: Hearing Before the Subcomm. on Commerce, Trade, and Consumer Prot.*, 109th Cong. (2005) (testimony of James Christian).

236. Tiger Webb, *3D Barcodes May Stop Counterfeits*, THE SCIENCE SHOW (Oct. 13, 2015), <http://www.abc.net.au/radionational/programs/scienceshow/3d-barcodes-counterfeit-goods/6850820>.

237. Perks, *supra* note 10.

238. Kalyanaraman, *supra* note 57, at 60.

239. *What is Spectroscopy?*, UNIVERSITY OF ARIZONA (last visited Feb. 7, 2016), http://loke.as.arizona.edu/~ckulesa/camp/spectroscopy_intro.html.

240. Kalyanaraman, *supra* note 57, at 60.

241. See *id.* at 60–61.

to patients. Innovation in tracking and identifying medication allows the industry to stay a step ahead of counterfeiters seeking to profit from the industry's development efforts.²⁴² Manufacturers of biologics take on these efforts to protect their goodwill and ensure patients can trust the medications they are taking.²⁴³

VIII. RECENT DEVELOPMENTS

“A major objective is for countries to agree that counterfeiting is a crime against human security and incorporate that principle into their laws,” said Dr. Howard Zucker, WHO Assistant Director-General for Health Technology and Pharmaceuticals.²⁴⁴ Identifying weaknesses in monitoring and tracking shipments through international commerce is also increasingly important in the global marketplace. After the Avastin counterfeit case, the world moved to improve drug monitoring and secure the supply chain responding to the growing counterfeit trade. Penalties for medicinal counterfeiting in Europe and the U.S. have addressed this need and are included in recent legislative developments.

In 2013, the Drug Supply Chain Security Act (DSCSA) was signed into law in the U.S.²⁴⁵ The new federal legislation preempts all state law, regulations, and requirements for tracing pharmaceuticals through the supply chain, creating a unified American system.²⁴⁶ The DSCSA requires the FDA to implement a national track-and-trace system in which manufacturers must attach product identifiers, such as bar codes, to each package or case of pharmaceutical product intended for the supply chain.²⁴⁷

Under the DSCSA, participants in the pharmaceutical supply chain, including distributors, dispensers, and repackagers, must develop

242. See Moran, *supra* note 231.

243. *Id.*

244. World Health Org., *WHO and partners accelerate fight against counterfeit medicines* WHO.INT (Nov. 15, 2006), <http://who.int/mediacentre/news/releases/2006/pr69/en/>.

245. Drug Quality and Security Act, Pub. L. No. 113–54, 127 Stat. 587 (2013) (to be codified in 21 U.S.C. § 301 et seq.); Bikash Chatterjee, *Serialization and the Drug Quality & Security Act*, PHARMACEUTICAL MANUFACTURING (Jan. 20, 2015), <http://www.pharmamanufacturing.com/articles/2015/serialization-drug-quality-security-act/>.

246. Bikash Chatterjee, *Serialization and the Drug Quality & Security Act*, PHARMACEUTICAL MANUFACTURING (Jan. 20, 2015), <http://www.pharmamanufacturing.com/articles/2015/serialization-drug-quality-security-act/>.

247. McGuireWoods, *Legal Alert: Drug Quality and Security Act* (Dec. 4, 2013), <https://www.mcguirewoods.com/Client-Resources/Alerts/2013/12/Drug-Quality-and-Security-Act.aspx>.

authentication methods to determine the legitimacy of pharmaceutical products under their control.²⁴⁸ The new law requires prompt FDA notification of illegitimate products.²⁴⁹ Upon determining a counterfeit product is present, participants in the secure drug supply chain must notify not only the FDA, but trading partners as well, preventing further circulation of compromised medication.²⁵⁰ The DSCSA also requires FDA notification if counterfeiting is suspected, but not verified.²⁵¹ Violations of the DSCSA are criminal in nature.²⁵² Counterfeit traffickers face up to 10 years in prison and up to \$2 million dollars in fines.²⁵³

The DSCSA is implemented in phases over the next decade.²⁵⁴ The first steps are improving traceability and documentation of pharmaceutical lots in the supply chain.²⁵⁵ The legislation emphasizes the “pedigree” model of tracing pharmaceuticals.²⁵⁶ Products are serialized, aggregated, and authenticated at each change in custody.²⁵⁷ This information is shared by trading partners in the supply chain.²⁵⁸ The weakness to this model is that counterfeits could enter the supply chain at any point from multiple distribution centers.²⁵⁹ In the final phases, the supply chain system will be able to track a specific pharmaceutical product all the way back to the manufacturer, thus addressing this problem.²⁶⁰

Europe is taking similar measures to secure the pharmaceutical supply chain. The E.U. strengthened the European supply chain in 2013 with

248. *Id.*

249. Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. § 582(b)(4)(B) (2015).

250. *See Are You Ready for the Drug Supply Chain Security Act?*, U.S. FOOD AND DRUG ADMINISTRATION [FDA], <http://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm427033.htm> (last updated Mar. 1, 2016).

251. *See* Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. § 360bbb-7 (2016).

252. *See E-Alert: Food & Drug*, COVINGTON & BURLING LLP, 22 (Aug. 10, 2012), https://www.cov.com/files/Publication/0c4b516e-d83a-4f48-9d34-1144bc0e3f90/Presentation/PublicationAttachment/773cafe3-f4c8-48fa-be2b-1fd0a9fcbd11/FDA_Safety&Innovation_Act_2012.pdf.

253. *Id.*

254. Brian Daleiden, *Protecting Patient Safety and the Drug Supply Chain Security Act (DSCSA)*, BECKER'S HOSP. REV. (Sept. 2, 2015), <http://www.beckershospitalreview.com/quality/protecting-patient-safety-and-the-drug-supply-chain-security-act-dscsa.html>.

255. *Id.*

256. Heather Zenk, *Understanding the Drug Supply Chain Security Act and How it Impacts Your Pharmacy*, AMERICAN SOCIETY FOR AUTOMATION IN PHARMACY 5 (June 25–27, 2015), http://www.asapnet.org/files/June2015/Presentations/ASAPJune15_Presentation_09_Zenk.pdf.

257. Chatterjee, *supra* note 246.

258. *Id.*

259. *Id.*

260. ENVIRONMENTAL XPRT, *Policy Management – DCSCA – Drug Supply Chain Integrity* (July 22, 2015), <http://www.environmental-expert.com/articles/policy-management-dscsa-drug-supply-chain-integrity-571661>.

amendments to the Falsified Medicines Directive.²⁶¹ Additional notification and documentation measures are required of supply chain participants.²⁶² Wholesalers are required to notify authorities if falsified product is suspected²⁶³ and to record pharmaceutical batch information.²⁶⁴ Member nations are required to report incidents to an E.U. database and remove suspected counterfeits from the supply chain.²⁶⁵ The directive obliges member nations to each set criminal penalties that are effective and dissuasive.²⁶⁶

According to the Council of Europe (COE), “[I]ncidences of counterfeit medical products and similar crimes undermine public trust in healthcare systems and authorities’ surveillance . . .”²⁶⁷ To this end, the COE Convention on the Counterfeiting of Medical Products and Similar Crimes involving threats to Public Health (Medicrime Convention) took effect in January 2016.²⁶⁸ The COE is a pan-European political organization including 47 member states.²⁶⁹ At least 24 member nations have signed or ratified the Medicrime Convention signaling a willingness for criminal enforcement

261. Council Directive 2011/62/EU of 8 June 2011, amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, as regards the Prevention of the Entry into the Legal Supply Chain of Falsified Medicinal Products, 2011 O.J. (L174) 74 (EC).

262. Sonja Seeberger, *The New Falsified Medicine Directive 2011/62/EU and Its Requirements for Stakeholders* (2012) (unpublished Master’s dissertation, University of Bonn) (available online at http://dgra.de/media/pdf/studium/masterthesis/master_seeberger_s.pdf).

263. Council Directive 2011/62/EU of 8 June 2011, amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, as regards the Prevention of the Entry into the Legal Supply Chain of Falsified Medicinal Products, art. 80(i), 2011 O.J. (L174) 74 (EC).

264. Council Directive 2011/62/EU of 8 June 2011, amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, as regards the Prevention of the Entry into the Legal Supply Chain of Falsified Medicinal Products, art. 80(e), 2011 O.J. (L174) 74 (EC).

265. Seeberger, *supra* note 262, at 42.

266. Council Directive 2011/62/EU of 8 June 2011, amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use, as regards the Prevention of the Entry into the Legal Supply Chain of Falsified Medicinal Products, art. 118(a), 2011 O.J. (L174) 74 (EC); *see also* Seeberger, *supra* note 262, at 43–44.

267. Catherine Saez, *Medicrime Convention Against Counterfeit Drugs To Enter Into Force In 2016*, INTELLECTUAL PROPERTY WATCH (Jan. 10, 2015), <http://www.ip-watch.org/2015/10/01/medicrime-convention-against-counterfeit-drugs-to-enter-into-force-in-2016/>.

268. COUNCIL OF EUROPE [COE], Press Release – DC123(2015) (Sept. 24, 2015), <https://wcd.coe.int/ViewDoc.jsp?id=2362047&Site=DC&BackColorInternet=F5CA75&BackColorIntranet=F5CA75&BackColorLogged=A9BACE>.

269. COUNCIL OF EUROPE [COE], *Maps & Members*, <http://www.coe.int/en/web/tbilisi/the-coe/objectives-and-missions> (last visited Feb. 1, 2016).

of counterfeiting crimes.²⁷⁰ The Medicrime Convention is a binding international instrument.²⁷¹

The broad scope of the Medicrime Convention leaves individual nations to fill legislative gaps.²⁷² For example, the treaty states, “Each Party shall take the necessary legislative and other measures to establish as offences under its domestic law,” which leaves room for varying interpretations.²⁷³ The Medicrime Convention sets out a framework for international and interagency cooperation, encouraging the sharing of data with both government and private agencies,²⁷⁴ and establishing counterfeiting offenses and addressing documentation issues.²⁷⁵ The COE measures aim to ensure compatibility between E.U. and non-E.U. nations while providing the flexibility needed to implement such system.²⁷⁶

Pharmaceutical tracking systems in Europe follows an “authentication” model.²⁷⁷ This model uses item-level serialization, database registration, and authentication at the point of dispensation.²⁷⁸ Both the pedigree and authentication model require further covert means of anti-counterfeiting technology to be fully effective.²⁷⁹

Global efforts to manage the supply chain are reactions to the ingenuity of counterfeiters threatening a previously robust system that is increasingly interconnected. Legislation is frequently implemented in phases that may take decades to fully take effect.²⁸⁰ For example, the Drug Supply Chain Security Act will be phased in over a period of 10 years.²⁸¹ The comprehensive statute requires guidance to be established for information exchange, product identification, package tracking, and evaluation of the

270. COE, *supra* note 268.

271. *Id.*

272. Susanne Keitel, MD, *The MEDICRIME Convention: criminalising the falsification of medicines and similar crimes*, GENERICS AND BIOSIMILARS INITIATIVE J. 138, 139 (2012), <http://gabi-journal.net/the-medicrime-convention-criminalising-the-falsification-of-medicines-and-similar-crimes.html>.

273. Council of Europe: Convention on the counterfeiting of medical products and similar crimes involving threats to public health [hereinafter MEDICRIME Convention] COE 211, art. 6 (Oct. 28, 2011).

274. MEDICRIME Convention, art. 1, 17.

275. COUNCIL OF EUROPE [COE], *The MEDICRIME Convention* (last visited Feb. 7, 2016), <https://www.edqm.eu/en/the-medicrime-convention-1470.html>.

276. COUNCIL OF EUROPE [COE], *FAQ eTACT – What You Should Know About eTACT* (last visited Feb. 7, 2016), <https://www.edqm.eu/en/FAQ-eTACT-1482.html>.

277. Chatterjee, *supra* note 246.

278. *Id.*

279. *Id.*

280. *See id.*

281. FDA, *supra* note 250.

system with targeted goals for different stakeholders implemented in stages.²⁸² Vigilance and deterrence are required to maximize pharmaceutical safety and protect patients that rely on life-saving treatments.

IX. RECOMMENDATION

“We don’t have the necessary data or surveillance to effectuate meaningful public health interventions or policy change,” said Tim Mackey, author and professor at the University of California, San Diego.²⁸³ Standardization and communication are essential to a secure international pharmaceutical supply chain. A global central authority is needed to coordinate international counterfeiting information. While different regional strategies will be used to suit legislative and enforcement needs of individual nations, a unifying program bringing data from various track and trace programs is needed to detect the international movement of counterfeits.

There must also be an incentive for those in possession of potential counterfeits to investigate the products without financial detriment. Red flags, such as purchasing at deep discounts and suspect packaging, give a possessor using reasonable care constructive knowledge of a counterfeit. However, without harsher penalties for counterfeit suppliers, there is little deterrent effect by any regulatory scheme. There are many broad solutions discussed to address the problem.²⁸⁴ The following recommendations set up a framework to achieve these objectives.

First, the WHO should take the lead and coordinate compulsory reporting of counterfeiting events to the WHO. There must be a central point of worldwide authority entrusted with surveillance of counterfeit medications and biologics. A centralized reporting system will remove international information gaps where counterfeiters flourish.

In conjunction with amendments to the Certification Scheme and a WHO reporting system program incorporating the various data already

282. *Id.* (presenting DSCSA deliverables timeframes); *see also* U.S. FOOD AND DRUG ADMINISTRATION [FDA], CDER Small Business and Industry Assistance (CDER SBIA) Webinar on The Drug Supply Chain Security Act, <http://www.fda.gov/Drugs/Development/ApprovalProcess/SmallBusinessAssistance/ucm388150.htm> (last updated Oct. 5, 2015) (explaining drug regulation and key aspects of the DSCSA).

283. Perks, *supra* note 10.

284. Jessica A. Ritsick, *Don't Call It a Counterfeit, and Other Recommendations From the IOM Report on Falsified and Substandard Drugs*, FDA LAW BLOG (Feb. 15, 2013), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/02/dont-call-it-a-counterfeit-and-other-recommendations-from-the-iom-report-on-falsified-and-substandar.html.

collected around the world, the WHO would require mandatory notification to the WHO of counterfeits identified in the supply chain by WHO nations. Non-WHO members would also be encouraged to report counterfeit events further supplementing the reporting system. The program would also incorporate track and trace data from nations and private sources. Some have noted such a database would also include pharmaceutical license suspensions.²⁸⁵

With notification requirements and a transparent reporting system assessable to partners, the WHO, in monitoring the reporting system, would have greater power to facilitate international cooperation and enforcement. Trend analysis and policy recommendations stemming from comprehensive data gathering could more precisely identify supply chain paths the counterfeits are taking across borders.

A WHO reporting system would not supersede national drug authorities' mandate to police pharmaceutical trade and establish regulations. Rather the WHO must act to bring together information from regional systems into a comprehensive package. The WHO in such a program could further evaluate the differences between the European model and the DSCSA requirements for tracking and pedigree documentation. A central program must overcome the difficulties of data analysis in different surveillance systems.²⁸⁶

The dual models of tracking pharmaceutical inventory will not prove to be mutually exclusive where counterfeits are concerned. A broad WHO reporting system inclusive of currently gathered data would increase international communication. Efforts at a web-based system are in progress at the WHO.²⁸⁷ A WHO system must incentives both Member States and other entities to report collected data.

As seen in the Avastin case, counterfeits were repeatedly sold through the same importation channels. Identification of these channels would have led to targeted inspections and prevented subsequent batches of fake Avastin from reaching cancer patients. In this case, River East Supplies in the U.K. would have been identified by the WHO and inspected by U.K. authorities in conjunction coordinated international support. Discrepancies in the importation paperwork, misleading sources of the drugs, and notification from medical professionals could have been reported to and detected by the WHO. The original counterfeit manufacturing sources could have been tracked down and the counterfeit inventory spread throughout the supply chain quarantined. Once the supply chain was secured, problems with importation paperwork and regulatory compliance could be remedied and

285. *Id.*

286. Perks, *supra* note 10.

287. Mackey, *supra* note 6, at 65.

appropriate measures taken by local regulatory authorities in accordance with local guidelines.

With the WHO on the forefront of coordinated reporting of counterfeiting, a globalized surveillance authority could track counterfeit pharmaceuticals. With international cooperation, individual nations would have the freedom to enforce their laws using information and support gathered from the WHO. Mandatory notification of counterfeits identified and the methods of importation increase transparency and catch counterfeiters, and their enabling suppliers, responsible for tainting the supply chain.

Second, the WHO should implement a purchase back and testing program for suspicious medication. By purchasing questionable pharmaceuticals from doctors, distributors, and wholesalers, the WHO can directly test drugs for authenticity. Counterfeit medicines around the globe kill over one million people annually.²⁸⁸ Managing a testing program facilitates WHO mission objectives to strengthen health services and establishing standards for safe medicines.²⁸⁹ The effects of a testing program are described below. Such a program would be cost effective given the \$18 billion in lost profits alone.²⁹⁰ There are also additional savings worldwide to public health agencies in terms of improved patient outcomes.

Pharmaceutical testing and adulterant screening is a public health harm reduction service with proven effectiveness in illicit markets.²⁹¹ For example, in the Netherlands an ecstasy monitoring program monitored the levels of MDMA found in the illegal street drug.²⁹² The program found that ecstasy tainted with dangerous drugs such as speed exited the market after warning campaigns.²⁹³ Other research shows that illicit market samples begin corresponding to the expected ingredients when pill-testing results are

288. Natalie Southwick, *Counterfeit Drugs Kill 1 Mn People Annually: Interpol*, INSIGHT CRIME (Oct. 24, 2013), <http://www.insightcrime.org/news-briefs/counterfeit-drugs-kill-1-million-annually-interpol>.

289. *Trade, Foreign Policy, Diplomacy and Health*, WORLD HEALTH ORG., <http://www.who.int/trade/en/> (last visited Feb. 28, 2016).

290. Irwin A. Blackstone, Ph.D. et al., *The Health and Economic Effects of Counterfeit Drugs*, AMERICAN HEALTH AND DRUG BENEFITS (June 2014), <http://www.ahdbonline.com/issues/2014/june-2014-vol-7-no-4/1756-the-health-and-economic-effects-of-counterfeit-drugs>.

291. Alison Ritter, *Six Reasons Australia Should Pilot 'Pill Testing' Party Drugs*, THE CONVERSATION (Nov. 11, 2014, 2:31 PM), <http://theconversation.com/six-reasons-australia-should-pilot-pill-testing-party-drugs-34073>.

292. Inge P. Spruit, *Monitoring Synthetic Drug Markets, Trends, and Public Health*, 36 SUBSTANCE USE & MISUSE 23, 24 (2001), <http://www.tandfonline.com/doi/full/10.1081/JA-100000227>.

293. *Id.* at 37–38.

known.²⁹⁴ The WHO buy-back type program would provide options to submit single samples for testing and be reimbursed for the sample purchase price. Reimbursement is critical due to the high cost of biologics. Health care providers must not be discouraged from pursuing dubious pharmaceuticals because it is financially burdensome to do so.

A centralized purchase back program is needed because some counterfeits, when recalled by a distributor, are simply resold to another buyer and make their way back to patients.²⁹⁵ A guaranteed reimbursement by the WHO prevents counterfeits from silently returning to the supply chain. The program would give the WHO more control in identifying counterfeit “hot spots.”

Had a purchase back system been in place in 2012, authorities may have noticed much sooner that East River Supplies, Richard’s Services, and CanadaDrugs were major sources of counterfeits. In the Avastin case, nurses and medical staff questioned the legitimacy of the drugs in their possession because the packaging was suspect.²⁹⁶ The ability to submit the samples for testing through a purchase back program would have provided 1) a definitive answer to the doctor from the WHO about the exact nature and condition of the potential counterfeit, and 2) by using a purchase back mechanism the doctor would not lose money and be able to stay in the business of providing patient care while a qualified agency entity validated safety.

Due to the high cost of biologics, doctors may only purchase limited amounts of the drugs for their patients.²⁹⁷ Sick patients need the drugs right away, but caregivers cannot take a chance on dubious pharmaceuticals. The WHO could exchange legitimate drugs rather than make a payment for the tested dose. Such exchanges facilitated in conjunction with national regulatory authorities ensure the appropriate local laws are followed. A quick exchange through local channels ensures patient care continuity.

In identifying counterfeits, the WHO would also send notice to the appropriate regulatory authorities of the need for auditing and inspection of the supply networks importing counterfeits. The results of drug testing would be input into the reporting system for further sharing of information among agencies and health care providers.

Third, the DSCSA must be amended to include personal injury liability for knowingly compromising the supply chain. When sellers ship biologic

294. An Inventory of On-Site Pill-Testing Interventions in the EU, at 55, EMCDDA (2001).

295. Horton, *supra* note 144.

296. See, e.g., Bill Berkot, *Doctors scour drug supplies after fake Avastin found*, REUTERS (Feb. 15, 2012, 7:40 PM), <http://www.reuters.com/article/us-avastin-idUSTRE81F03220120216>.

297. James C. Robinson, *Insurers’ Strategies for Managing the Use and Cost of Biopharmaceuticals*, 25 HEALTH AFFAIRS No. 5 1205, 1206, 1209 (2006).

medication outside of specified storage requirements, such as a refrigerated temperature, they should be liable for patient harm for knowingly compromising and endangering patient safety.²⁹⁸ Supply chain participants using reasonable care under the circumstances have constructive knowledge of the counterfeits. Furthermore, physicians that knowingly continue to purchase counterfeit products and have direct knowledge of adverse patient events should be subject to increased penalties for assault and battery of their patients.²⁹⁹ In spite of the difficulties in proving that a drug administered to patients was counterfeit, actual harm in the case of biologics can be presumed. Doctors and distributors that knowingly conceal pharmaceutical shipments by falsifying documents to avoid customs confiscation are complicit in illegal distribution. They must be held accountable to patients harmed by their actions.

Patient harm can be presumed because counterfeits compromise a sick person's chance to receive treatment and recover. By not receiving the appropriate treatment, a patient is harmed with continued illness. Worse, counterfeits may harm patients, but the effects could be perceived as part of the preexisting condition. Patients may never know they did not receive the right medication and that the side effects are not normal or expected.

None of the counterfeit Avastin legal claims directly related to personal injury associated with patient safety and adverse events.³⁰⁰ Currently, importation of unapproved pharmaceuticals in the U.S. is a strict liability offense.³⁰¹ Anyone in a position of responsibility may be prosecuted for introducing an adulterated drug into interstate commerce.³⁰² But, there is no enforcement beyond the most egregious offenses.³⁰³ For example, in

298. See *Contract Pharma Presents Strategies for Mitigating Risk and Ensuring Compliance in the Biomaterial Cold Chain*, BIO STORAGE TECHNOLOGIES, <http://www.biostorage.com/news-articles/contract-pharma-presents-strategies-for-mitigating-risk-and-ensuring-compliance-in-the-biomaterial-cold-chain/>; see also 21 CFR § 250.50(a)(2) (codifying the need to ensure proper refrigeration during transportation when needed).

299. See Press Release, Dept. of Justice, *supra* note 33; see also Howard Sklamberg, Deputy Comm'r for Glob. Regulatory Operations & Policy, Food & Drug Admin., Speech Before the Committee on Energy and Commerce: Counterfeit Drugs: Fighting Illegal Supply Chains (Feb. 27, 2014).

300. Mackey, *supra* note 97, at 303.

301. Importation of Drugs, U.S. FOOD AND DRUG ADMINISTRATION [FDA], <http://www.fda.gov/ForIndustry/ImportProgram/ucm173751.htm> (last updated Sept. 25, 2015).

302. 21 U.S.C. § 331 (2016).

303. See, e.g., Press Release, U.S. Attorney's Office, Federal Jury Convicts Greenville Oncologist and Practice Manager of Violating Food, Drug and Cosmetic Act (Dec. 16, 2013), <http://www.justice.gov/usao-edtn/pr/federal-juryconvicts-greenvilleoncologist-and->

2008 an Arizona couple pled guilty to selling counterfeit drugs made in India through an online pharmacy making millions of dollars on over 600 brand names sold at deep discounts.³⁰⁴ In 2014, three people in Texas were charged with smuggling over 100,000 counterfeit pills into the U.S.³⁰⁵ The Chinese supplier allegedly paid the defendants involved in the conspiracy.³⁰⁶

Finally, the WHO Certification Scheme should also be amended to include a minimum recommended penalty for lack of due diligence when importing drugs through the gray market. Supply chain participants should know that when they purchase medications with substantial discounts that the medications carry a substantial risk of adulteration. The potential for patient harm is inferred from the circumstances surrounding importation from the gray market and unlicensed sources.

Marketing efforts that have a higher risk of counterfeiting fraud, such as fax and email blasts sent from ambiguous sources, are a red flag to distributors and doctors that they are purchasing fraudulent products and counterfeits. New track and trace requirements in the U.S. and E.U. may reduce these types marketing techniques.

The WHO provides guidance on health policy.³⁰⁷ By setting a penalty standard for neglecting due diligence the WHO will continue to be a leader healthcare policy. Establishing this guidance encourages others to do the same.

These recommendations accomplish the goals necessary to prevent counterfeit pharmaceuticals from reaching patients. Through international communication, purchase and testing programs, and increased penalties, the supply chain becomes more secure. These changes contain both preventive and deterrent effects to counterfeiting.

practicemanager-violating-fooddrug (oncology doctors were convicted of purchasing over \$3 million in counterfeit medications and billing Medicaid to increase their profits).

304. Bob Christie, *Lake Havasu Pair Indicted in Internet Drug Scheme*, AZCENTRAL (Jul. 6, 2008, 12:00 AM), <http://www.azcentral.com/news/articles/2008/07/06/20080706drugs0706.html>; see eAlert, Hughes Hubbard, Rare Criminal Prosecution Highlights Sales of Illegal and Counterfeit Drugs in the United States 2–3 (Apr. 2009), [http://www.hugheshubbard.com/PublicationDocuments/Rare%20Criminal%20Prosecution_april 2009.pdf](http://www.hugheshubbard.com/PublicationDocuments/Rare%20Criminal%20Prosecution_april%202009.pdf) (There are a number of legal theories for prosecution; analysis is fact specific. Civil proceedings are also available to manufacturers.).

305. Press Release, Dept. of Justice, Three Indicted in Prescription Drug Smuggling Ring (Oct. 6, 2014), <http://www.justice.gov/opa/pr/three-indicted-prescription-drug-smuggling-ring>.

306. U.S. v. Giddens, No. 6:14-CR-49 (E.D. TX, Aug. 27, 2014), <http://www.justice.gov/file/69751/download>.

307. WHO, *supra* note 289.

X. CONCLUSION

The biopharmaceutical supply chain is a prime target for criminals seeking to profit off the weak and desperate. No one change will completely ensure healthcare system safety. An inclusive approach must be utilized. Counterfeiters must be discouraged at all points in international commerce. Detection and deterrence are critical factors.

Biopharmaceuticals are important medications treating debilitating diseases that do not respond to traditional drugs. Because biologic treatments are expensive, there is abundant incentive to counterfeit these drugs. Tampering and diluting of biologics is often undetectable, necessitating the need for a comprehensive, international approach.

Counterfeits may cross many borders and change hands several times before reaching the patients they are meant to treat. Immediate action and cooperation by individual countries is needed to ensure there are appropriate safety measures at each link in the supply chain. Many nations have implemented through laws to address the problem, however, a unified international approach is needed to be successful.

Penalties for counterfeiters must have deterrent value to discourage trade in fake medications. Importers, distributors, and physicians purchasing what they hope is legitimate medication cannot be allowed to dissemble about the quality of questionable medicines. Many times fake drugs are easily identifiable with cursory diligence. There must be consequences to willful blindness when importers have reason to know it is likely they have counterfeits. There must also be an incentive component to the approach facilitating reporting of counterfeit events.

With a streamlined and unified international approach guided by the WHO, the biopharmaceutical supply chain can be secured. It is a public health priority for the safety of patients who need these drugs the most and will literally die without these lifesaving treatments.

