
**INTERNATIONAL PHARMACEUTICAL MISTRIALS:
EXISTING LAW FOR THE PROTECTION OF
FOREIGN HUMAN SUBJECTS AND A
PROPOSAL FOR REFORM**

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ABSTRACT

The cost of developing a new drug has grown to nearly one billion dollars in the United States. Conducting these trials abroad is much more lucrative for pharmaceutical companies.

Federal law and U.S. consumers rightly demand safe and efficacious drugs. But there is a growing trend of outsourcing clinical testing to poor and developing countries to fuel America's ever-increasing demand for pharmaceuticals. Although testing abroad does provide some advantages to clinical subjects in the developing world, reform is necessary to protect these vulnerable populations. Over the last twenty years, two divergent pharmaceutical regulatory regimes have arisen: a robust domestic system and a weak foreign one. Currently, federal law regulating U.S. pharmaceutical companies' clinical testing abroad is ambiguous, leaving foreign clinical subjects without adequate legal and medical protections and leaving them little recourse if they are injured.

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While a recent Second Circuit decision allowed injured Nigerians to recover under the Alien Tort Statute, this note argues that the court exceeded the Supreme Court's narrow interpretation of this law. In order to protect the human beings that help make many life-saving drugs a reality, the U.S. should reform federal law to increase informed consent requirements, boost FDA oversight of foreign trials, create civil and criminal penalties similar to those contained in the Foreign Corrupt Practices Act, and provide a limited forum to compensate those injured abroad by U.S. drug companies.

I. INTRODUCTION

Adam Novak, a Hungarian bartender in his mid-twenties suffering from schizophrenia, had been confined to the Kutvolgyi Uti Hospital psychiatric unit in Budapest for two weeks when a doctor asked him to participate in a test of the drug Aripiprazole.¹ The researcher who recruited Novak for the Bristol-Myers sponsored trial later stated, "It is easier to find patients here . . . [P]atients in western countries—and in the United States especially—have an overdeveloped sense of their rights and a fear of being harmed."² Indrek Kelder, an Estonian accountant, was recruited for a trial in distant Switzerland by a pharmaceutical research company on behalf of leading drug companies.³ After he received free plane tickets and roughly one month's salary, Kelder signed consent forms in German, a language that he could not read.⁴ Swiss authorities later shut down the clinic to which Kelder was sent after discovering that the company was conducting trials on scores of drug addicts, refugees and others ignorant of their status as clinical trial subjects.⁵

Unfortunately, these incidents, which would immediately raise profound ethical, legal and regulatory issues in the United States,⁶ are not isolated infractions.⁷ Rather, they are part of a larger trend⁸ whereby U.S. and western drug manufacturers increasingly conduct clinical trials

¹ Sharon LaFraniere, et al., *The Dilemma: Submit or Suffer; 'Uninformed Consent' Is Rising Ethic of the Drug Test Boom*, WASH. POST, Dec. 19, 2000, at A1.

² *Id.*

³ *Id.*

⁴ *Id.*

⁵ *Id.*

⁶ See 45 C.F.R. § 46.101 (2009).

⁷ See generally Amy F. Wollensack, *Closing the Constant Garden: The Regulation and Responsibility of U.S. Pharmaceutical Companies Doing Research on Human Subjects in Developing Nations*, 6 WASH. U. GLOBAL STUD. L. REV. 747, 747-48 (2007).

⁸ The Tufts University Center for the Study of Drug Development predicted that 65% of clinical trials will be conducted abroad in the near future. Carolyne R. Hathaway et al., *Looking Abroad: Clinical Drug Trials*, 63 FOOD & DRUG L. J. 673, 674 (2008).

in developing states, rather than in the U.S. and other developed nations.⁹ The reasons for this shift in pharmaceutical clinical trials are complex, but mainly relate to economics and government oversight.

Conducting these trials abroad is better for pharmaceutical companies' bottom line. The cost of developing a new drug has grown to nearly one billion dollars in the United States.¹⁰ Those costs include conducting initial research, completing three phase trials involving human volunteers, and obtaining preliminary Food and Drug Administration ("FDA") approval through the investigational new drug ("IND") permit.¹¹ By transferring costly trials to countries with far fewer regulatory hurdles, a pharmaceutical company can gain significant savings.

More specifically, simply finding the requisite number of human subjects necessary to gain the FDA's coveted New Drug Application ("NDA") approval is much less expensive in poorer nations.¹² Many Americans are unwilling to participate in possibly dangerous clinical trials where they may receive a placebo. Additionally, for a variety of reasons, doctors often do not recommend or even mention clinical trials to their patients.¹³ In contrast, many citizens of poorer nations, such as India, lack access to effective healthcare and view the chance to participate in a clinical trial as a "healthcare windfall."¹⁴ Also, in post-Soviet states, there is an existing medical infrastructure, with enthusiastic, underpaid doctors eager to gain a bounty for recruiting subjects.¹⁵ Finally, people with a given disease or condition in the developing world are less likely to have been treated for that condition, making them more suitable for participation in a drug trial.¹⁶

⁹ DEP'T OF HEALTH & HUMAN SERV., OFFICE OF INSPECTOR GENERAL, OEI-01-00-00190, THE GLOBALIZATION OF CLINICAL TRIALS: A GROWING CHALLENGE IN PROTECTING HUMAN SUBJECTS, 6 (2001) [hereinafter *HHS IG Report*] (calculating the growth in foreign clinical trials in previous decade at 1600%).

¹⁰ Darius Kharabi, *A Real Options Analysis of Pharmaceutical-Biotechnology Licensing*, 11 STAN. J.L. BUS. & FIN. 201, 204 (2006).

¹¹ Christopher W. Anderson & Ying "Jenny" Zhang, *Security Market Reaction to FDA Fast Track Designations*, 37 No. 2 J. HEALTH CARE FIN. 27, 27-28 (2010).

¹² Michael J. Malinowski, *Ethics in a Global Pharmaceutical Environment*, 5 SANTA CLARA J. INT'L L. 57, 67 (2006).

¹³ James Cekola, *Outsourcing Drug Investigations to India: A Comment on U.S., Indian and International Regulation of Clinical Trials in Cross-Border Pharmaceutical Research*, 28 NW. J. INT'L L. & BUS. 125, 128 (2007).

¹⁴ See, e.g., *id.* at 129; see also Malinowski, *supra* note 12.

¹⁵ See Malinowski, *supra* note 12.

¹⁶ Cekola, *supra* note 13, at 129. This concept is known as "drug naïveté." *Id.* (regarding drug naïveté in India); see also Daniel W. Fitzgerald & Angela Wasunna, *Away from Exploitation and Towards Engagement: An Ethical Compass for Medical Researchers Working in Resource-Poor Countries*, 33 J.L. MED. & ETHICS 559, 560 (2005) (more generally regarding drug-naïveté in resource-poor countries).

This movement of trials to developing nations has important health benefits for patients in the U.S. and in the states where these trials are conducted.¹⁷ However, given that these poorer nations often do not have an effective regulatory or judicial infrastructure, trial subjects are at risk of severe exploitation and harm with little chance of compensation.¹⁸ These issues, which the *Washington Post* brought to the nation's attention in 2000 with its "Body Hunters" series,¹⁹ were addressed by the Second Circuit in *Abdullahi v. Pfizer*.²⁰ The case involved a group of Nigerian plaintiffs seeking damages under the Alien Tort Statute²¹ ("ATS") for injuries sustained during clinical trials of Pfizer's antibiotic Trovan.²²

Given the Supreme Court's narrow application and hesitancy to expand the ATS,²³ this note will argue that the ATS, as currently written, is neither an ideal vehicle for compensating aggrieved human subjects, nor an effective tool to change the behavior of American pharmaceutical companies conducting trials abroad. However, as cases such as *Abdullahi* highlight, due to ineffectual judicial systems in developing nations and without access to some adjudicative body, subjects that have been harmed by western pharmaceutical trials may be effectively foreclosed from any measure of justice.²⁴ As such, this note will argue that regulatory and legislative action in the United States would be most effective in protecting vulnerable subjects in foreign clinical trials while permitting U.S. drug companies to retain some of the economic advantages that foreign trials facilitate. In particular, this note will suggest a more robust role for the FDA in ensuring that foreign clinical trials for drugs marketed in the U.S. provide adequate protections for human subjects, combined with a new statutory scheme similar to the Foreign Corrupt Practices Act ("FCPA"). At the same time, because of the limited investigative resources of the FDA and the globalized nature of the pharma-

¹⁷ Adam H. Laughton, *Somewhere to Run, Somewhere to Hide?: International Regulation of Human Subject Experimentation*, 18 DUKE J. COMP. & INT'L L. 181, 202-204 (2007).

¹⁸ See Samantha Evans, *The Globalization of Drug Testing: Enforcing Informed Consent Through the Alien Tort Claims Act*, 19 TEMP. INT'L & COMP. L.J. 477, 479 (2005).

¹⁹ See Joe Stephens, *The Body Hunters: Exporting Human Experiments; Where Profits and Lives Hang in Balance; Finding an Abundance of Subjects and Lack of Oversight Abroad, Big Drug Companies Test Offshore to Speed Products to Market*, WASH. POST, Dec. 17, 2000, at A1; see also Sonia Shah, *Globalizing Clinical Research*, THE NATION, July 1, 2002, at 23.

²⁰ *Abdullahi v. Pfizer*, 562 F.3d 163 (2d Cir. 2009), *cert. denied*, 130 S.Ct. 3541 (2010).

²¹ Alien's Action for Tort, 28 U.S.C. § 1350 (2006).

²² *Abdullahi v. Pfizer*, 562 F.3d at 163, 168-71 (describing the drug Trovan).

²³ See *Sosa v. Alvarez-Machain*, 542 U.S. 692, 721-22 (2004) (holding that court will take restrictive approach to ATS).

²⁴ Evans, *supra* note 18, at 479.

ceutical industry, Congress should amend the ATS to allow aliens to sue when the underlying action is capable of regulation by the FDA.

II. THE ALIEN TORT STATUTE AND FOREIGN CLINICAL TRIALS

A. *Background on the Alien Tort Statute*

The ATS, with a terseness that perhaps belies its complex application, reads, “The district courts shall have original jurisdiction of any civil action by an alien for a tort only, committed in violation of the law of nations or a treaty of the United States.”²⁵ To invoke the statute, the litigant must meet three necessary elements.²⁶ The litigant asserting a violation must be an alien and must also have a claim sounding in tort.²⁷ The third, and perhaps most thorny, requirement is that the party claiming a violation of the ATS must establish that “the tort [was] committed in violation of the law of nations or a treaty of the United States.”²⁸

Passed in 1789, the Act was largely dormant for almost two centuries.²⁹ In the contemporary context, the Act has mainly been used by victims of torture and other human rights violations against offending states.³⁰ Most recently, in 2004 the Supreme Court dealt with the third requirement of the ATS in *Sosa v. Alvarez-Machain*.³¹ The plaintiff, who the Drug Enforcement Agency (“DEA”) had previously suspected of complicity in torturing one of its agents, alleged that a Mexican national, working for the United States, had arbitrarily arrested him and brought him to the United States to face prosecution.³²

The Court held that the plaintiff did not satisfy the requirement that the tort alleged was a violation of the law of nations.³³ For the Court, Justice Souter reasoned that the ATS can only be used when the litigant alleges the violation of an international standard that the world’s nations

²⁵ 28 U.S.C. § 1350 (2006).

²⁶ 13D CHARLES ALAN WRIGHT & ARTHUR R. MILLER ET AL., FEDERAL PRACTICE AND PROCEDURE § 3585 (3d ed. 2009).

²⁷ *Id.*

²⁸ *Id.*

²⁹ *Id.* Its mysterious origins led the Second Circuit to call it a “kind of legal Lohengrin,” *id.*, after the mysterious Knight appearing in a boat drawn by a swan in Wagner’s opera. *Synopsis: Lohengrin*, THE METROPOLITAN OPERA, <http://www.metoperafamily.org/metopera/history/stories/synopsis.aspx?id=127> (last visited Jan. 22, 2011).

³⁰ *See, e.g.*, *Filartiga v. Pena-Irala*, 630 F.2d 876 (2d Cir. 1980) (finding torture by state violative of international norms); *Tel-Oren v. Libyan Arab Republic*, 726 F.2d 774 (D.C. Cir. 1984) (holding no jurisdiction in regards to PLO attack on bus); *Doe I v. Unocal Corp.*, 395 F.3d 932 (9th Cir. 2002), *vacated en banc*, 403 F.3d 708 (9th Cir. 2005) (concerning human rights violations in building of natural gas pipeline).

³¹ *Sosa v. Alvarez-Machain*, 542 U.S. 692, 698 (2004).

³² *Id.* at 697-98.

³³ *Id.* at 697.

have accepted and defined to the same degree as the few internationally-accepted norms existing at the passage of the ATS.³⁴ These international norms, Souter explained, as given by the lawgiver Blackstone, consisted of piracy, safe conduct violations and offenses against ambassadors.³⁵ Because Sosa's allegation of a brief arbitrary arrest did not "rest on a norm of international character accepted by the civilized world and defined with a specificity comparable to the features of the recognized 18th-century paradigms," he had no right of action under the ATS.³⁶ This holding, despite the fact that the U.S. was a signatory to a non-self-executing covenant banning arbitrary arrest, and despite the international community's wide acceptance of the Universal Declaration of Human Rights, which, the Court noted, "did not itself create obligations enforceable in the federal courts."³⁷ The Court was hesitant to inject itself into foreign policy, an arena that the Court views as best left to the political branches of government.³⁸ Also, the Court urged judicial caution when expanding international rights of action that were not expressly created by Congress.³⁹ While the Court left the ATS door "ajar,"⁴⁰ this case shows the extremely restrictive view that the Court will apply to a litigant seeking to expand the ATS to cover informed consent violations in foreign clinical trials.

B. *The ATS as Applied to Foreign Clinical Trials*

In *Abdullahi*, the plaintiffs, the guardians of several Nigerian children, sued Pfizer under the ATS in the Southern District of New York for violating customary international law norms.⁴¹ Specifically, the plaintiffs alleged that Pfizer had failed to obtain their informed consent before commencing the drug trial.⁴² The district court dismissed the case for lack of subject matter jurisdiction and in the alternative for *forum non*

³⁴ *Id.* at 725.

³⁵ *Id.* at 724.

³⁶ *Id.* at 725.

³⁷ *Sosa v. Alvarez-Machain*, 542 U.S. at 734-35. The covenant was the International Covenant on Civil and Political Rights, which the plaintiffs in *Abdullahi* also pointed to as evidence that informed consent was a sufficient international norm. *Id.*; see also *Abdullahi v. Pfizer*, 562 F.3d at 175.

³⁸ *Sosa v. Alvarez-Machain*, 542 U.S. at 727.

³⁹ *Id.* at 728.

⁴⁰ *Id.* at 729.

⁴¹ Danielle Cendrowski, *International Health Law Violations Under the Alien Tort Statute: Federal Appeals Court Reinstated Lawsuit Under the Alien Tort Statute Against United States Pharmaceutical Company Pfizer Brought by Nigerian Children and Their Guardians – Abdullahi v. Pfizer, Inc.*, 35 AM. J.L. & MED. 233 (2009); see also *Abdullahi v. Pfizer*, 562 F.3d at 168. In this case, the plaintiffs claimed informed consent was an international law norm. *Id.*

⁴² *Id.*

conveniens.⁴³ The plaintiffs' appeal was then consolidated with the appeal of several other Nigerian plaintiffs from a similar suit against Pfizer alleging violations of the ATS and two Connecticut state statutes.⁴⁴

In 1996, Pfizer researchers, after failing to find the requisite number of subjects necessary for FDA approval in U.S. clinical trials, flew to Kano, Nigeria to test their potential blockbuster antibiotic Trovafloxacin ("Trovan").⁴⁵ Pfizer chose Kano because of a local outbreak of meningitis in children which Pfizer wanted to gain FDA approval to treat with Trovan.⁴⁶ The plaintiffs alleged that, with the participation of the Nigerian government, three Pfizer researchers recruited two hundred sick children seeking treatment at the Kano Infectious Disease Hospital.⁴⁷ Allegedly, Pfizer gave half the child subjects Trovan, which previously showed potentially lethal side effects in animal tests, and administered an FDA-approved drug to the control group.⁴⁸ The children's guardians also claimed that Pfizer deliberately gave lower than optimal doses of the control drug to the children in order to skew the trial towards Trovan.⁴⁹ The plaintiffs also alleged that the investigators left Kano after two weeks, without providing any follow-up care for the test subjects.⁵⁰ Purportedly, eleven of the children involved in the trial died, while others suffered ghastly complications such as deafness and the inability to walk or talk.⁵¹

More specifically, the children's guardians claimed that the company's researchers failed to inform them or their children (the test subjects) of several material pieces of information.⁵² First, they contended, the researchers neglected to give the subjects any consent documents in English, which failed to conform to the investigators' own protocol.⁵³ Second, the company allegedly failed to notify the subjects that there was a non-experimental alternative treatment center in the same hospital run by the aid group Doctors Without Borders.⁵⁴ Third, along the informed consent vein, the Nigerians asserted that the researchers failed to alert the subjects to all the possible side effects of the antibiotic.⁵⁵ In addition

⁴³ *Id.*

⁴⁴ *Id.* The statutes were the Connecticut Unfair Trade Practices Act and the Connecticut Products Liability Act. *Id.*

⁴⁵ Joe Stephens, *Where Profits and Lives Hang in Balance; Finding an Abundance of Subjects and Lack of Oversight Abroad, Big Drug Companies Test Offshore to Speed Products to Market*, WASH. POST, Dec. 17, 2000, at A1.

⁴⁶ *Id.*

⁴⁷ *Abdullahi v. Pfizer*, 562 F.3d at 169.

⁴⁸ *Id.*

⁴⁹ *Id.*

⁵⁰ *Id.*

⁵¹ *Id.*

⁵² *Id.*

⁵³ *Id.* at 169-170.

⁵⁴ *Id.* at 170.

⁵⁵ *Id.*

to these allegations, the plaintiffs contended that Pfizer forged documents relating to the approval of a hospital review committee, and that several doctors, including one Pfizer doctor, condemned the experiments.⁵⁶

The Second Circuit, in an expansive holding, overturned the district court and held that informed consent was an international norm under *Sosa* and thus the plaintiffs had a right of action to sue under the ATS.⁵⁷ In its ruling, the appellate court reasoned that the Nuremberg Code, the Declaration of Helsinki, other international medical and political conventions and U.S. informed consent law were all indicative of an international norm akin to those norms accepted at the passage of the ATS.⁵⁸ While the court's analysis of the world's efforts demonstrates the value that the international community places on informed consent and provides a policy argument for extending the ATS, it does not meet the high bar that *Sosa* set. The appellate court's ruling fails to adequately take into account the Supreme Court's hesitancy to interfere with foreign relations and the Supreme Court's caution in implying private rights of action that Congress has not created. *Abdullahi*'s reasoning makes much of the various accords, agreements and conventions regarding medical experimentation and informed consent. However, when *Sosa*'s restrictive analysis is applied, these admirable standards look very much like the international framework and consensus that the Supreme Court found lacking. For the above reasons, the Second Circuit should not have expanded the ATS as currently written to aggrieved participants in international pharmaceutical trials.

⁵⁶ *Id.* Plaintiffs complained that while Pfizer claimed to have secured an approval letter from the hospital's ethics committee, this committee did not exist at the time the letter was written.

⁵⁷ *Id.* at 187.

⁵⁸ *Id.* at 177-84. Roughly speaking, there are four sets of international standards designed to protect human subjects in clinical trials. Benjamin Mason Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 BERKELEY J. INT'L L. 513, 526, 523-29 (2002). The Nuremberg code, developed during the trial of the infamous "Nazi Doctors," banned any human experimentation on incapacitated or incompetent individuals and required that researchers obtain the voluntary consent of subjects. *Id.* at 523-24. The Declaration of Helsinki was written by doctors and attempted to ease the strict requirements of the Nuremberg Code to increase medical innovation while still protecting subjects. *Id.* at 525-26. The Convention on Human Rights and Biomedicine ("CHR") was passed by the Council of Europe to protect human subjects from the burgeoning field of genetic research. *Id.* at 527-29. Finally, the WHO drafted the International Ethical Guidelines for Biomedical Research involving Human Subjects which lays out more specific guidelines in relation to the Helsinki Declaration. *Id.* at 526-27.

III. EXISTING REGULATORY CRITIQUE

As a regulator, the FDA arguably has historically been effective at conducting accurate cost-benefit analyses to decide whether a drug or medical device is sufficiently safe to enter interstate commerce.⁵⁹ While recent missteps, such as the Vioxx and Bextra scandals, have demonstrated agency error in letting harmful drugs come to the market, the FDA's historical hesitancy to allow dangerous, though potentially promising, drugs on the market is a more accurate critique.⁶⁰ As the FDA operates "with a great deal of autonomy from political and legal controls,"⁶¹ it is primarily a science-driven, bottom-up agency that is in an effective position to ensure drug safety.⁶² As such, this note argues that utilizing the existing structure of the FDA while increasing the agency's regulatory and oversight capabilities is one essential component to better protect human subjects in clinical trials abroad.

While this note is mainly concerned with the protection of human subjects, it is nevertheless crucial to understand the basics of how a chemical compound legally transforms from a mere hypothesis to a marketable drug. The first step in the process is for the sponsor of a new drug, such as a pharmaceutical company or an academic institution, to submit an investigational new drug application ("IND") to the FDA.⁶³ In the IND, the sponsor must provide information regarding studies of the product on animals, as well as the protocols and qualifications of the study and its researchers.⁶⁴ In addition, the IND must identify the composition of the Institutional Review Board ("IRB"), an independent body that must "assure the protection of the rights and welfare of the human subjects."⁶⁵ The FDA reviews this submission for approximately one month to ensure that the study complies with federal law, and if the agency does not object

⁵⁹ Jennifer A. Surprenant, *Should Preemption Apply in a Pharmaceutical Context? An Analysis of the Preemption Debate and What Regulatory Compliance Statutes Contribute to the Discussion*, 77 *FORDHAM L. REV.* 327, 357-58 (2008).

⁶⁰ See Cass R. Sunstein, *Administrative Substance*, 1991 *DUKE L.J.* 607, 625 (1991) ("By delaying the entry of beneficial drugs into the market, the Food and Drug Administration has dramatically increased risks to life and health in some settings."). For the most current critique in this vein, one need look no further than the constitutional litigation and publicity that ensued when the FDA refused to give 21 year old Abigail Burroughs access to experimental drug therapy. See generally Nicolas J. Plionis, *The Right to Access Experimental Drugs: Why the FDA Should Not Deprive the Terminally Ill of a Chance to Live*, 16 *WM. & MARY BILL RTS. J.* 901 (2008).

⁶¹ Gary Lawson, *Dirty Dancing—The Stumbles with the Chevron Two Step: A Response to Professor Noah*, 93 *CORNELL L. REV.* 927, 938 (2008).

⁶² Cf. David C. Vladeck, *Preemption and Regulatory Failure*, 33 *PEPP. L. REV.* 95, 101 (2005) (stating that FDA is "perhaps the most capable federal safety agency").

⁶³ See Investigational New Drug Application, 21 *C.F.R.* § 312.20 (2010).

⁶⁴ Cekola, *supra* note 13, at 132.

⁶⁵ Institutional Review Board, 21 *C.F.R.* § 56.101102(g) (2010).

to the application, the sponsor can begin drug trials.⁶⁶ The sponsor must then conduct clinical trials that are comprised of three phases.⁶⁷ In the first phase, the drug is given to humans in escalating doses to determine the maximum safe dosages and side effects.⁶⁸ This phase is usually comprised of a small number of subjects, varying from about twenty to eighty volunteers.⁶⁹ The second phase of a trial usually consists of several hundred subjects and is designed to collect preliminary efficacy data as well as additional safety information.⁷⁰ Finally, phase three involves thousands of subjects and is “intended to gather the additional information about effectiveness and safety needed to evaluate the overall risk-benefit of the drug.”⁷¹ The FDA then uses this data to determine if the drug is granted the all-important New Drug Application (“NDA”) license, allowing the drug to be marketed in the U.S.⁷²

As detailed above, before a pharmaceutical company can begin its legally mandated three-phase trials, it must convince the FDA that these trials will be ethically and effectively designed and conducted. Currently, under federal law, the regulations that provide protections for human subjects in trials conducted in the U.S. are arguably more stringent than those relating to subjects in trials abroad.⁷³ In order to understand this disparity, this section will first explore the history and content of federal regulations governing clinical trials in the United States. This note will then utilize the law governing domestic research to elucidate the gap that leaves foreign clinical subjects with little protection, and even less ability to seek adequate compensation when FDA-regulated pharmaceutical companies injure them.

From a series of commissions and reports in the late 1970s, the most significant being *The Belmont Report*, the federal government enacted regulations governing research on humans, referred to as “The Common Rule.”⁷⁴ Mentioned earlier in this section, one of the hallmark federal mandates is the requirement that an IRB oversee each trial to ensure the

⁶⁶ Areta L. Kupchyk & Josephine M. Torrente, *R&D 101: Legal Issues During Research and Development*, in PHARMACEUTICAL LAW 2006: ACROSS THE PRODUCT LIFE CYCLE, 19 (2006).

⁶⁷ Cekola, *supra* note 13, at 133-34.

⁶⁸ *Id.* at 133.

⁶⁹ *Id.* at 132.

⁷⁰ Kupchyk & Torrente, *supra* note 66, at 21.

⁷¹ *Id.*

⁷² Emily Marden, *Open Source Drug Development: A Path to More Accessible Drugs and Diagnostics?*, 11 MINN. J.L. SCI. & TECH. 217, 240-41 (2010).

⁷³ See Robert Gatter, *Conflicts of Interest in International Human Drug Research and the Insufficiency of International Protections*, 32 AM. J. L. & MED. 351, 363 (2006).

⁷⁴ LAINIE FRIEDMAN ROSS, CHILDREN IN MEDICAL RESEARCH: ACCESS VERSUS PROTECTION, 63 (John Harris et al. eds., 2006); *see generally* 45 C.F.R. § 46.101 (2009).

protection of vulnerable subjects.⁷⁵ The IRB's duties are exhaustively spelled out in the federal code.⁷⁶ Yet perhaps most cogent in any discussion of human subject protections is the requirement of informed consent. 21 C.F.R. § 50.25 requires researchers to explain eight factors to volunteers: (1) the purpose, extent and procedures of the trial; (2) reasonably foreseeable risks; (3) expected benefits; (4) alternative procedures that may be advantageous to the patient; (5) confidentiality of the trial's records; (6) compensation for injuries; (7) a contact point for questions

⁷⁵ Protection of Human Subjects, 45 C.F.R. § 46.111(a)(3); *see also* 21 C.F.R. § 56.102(g) (2009).

⁷⁶ The following are the criteria that an IRB must use to approve research:

- (a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:
 - (1) Risks to subjects are minimized:
 - (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
 - (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
 - (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
 - (3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.
 - (4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by § 46.116.
 - (5) Informed consent will be appropriately documented, in accordance with, and to the extent required by § 46.117.
 - (6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
 - (7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- (b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

45 C.F.R. § 46.111.

about the research; and (8) the voluntary character of participation.⁷⁷ Finally, under what is known as “Subpart D,” federal law affords children even greater protections in research.⁷⁸ Generally, researchers must obtain parents’ consent as well as the child’s assent, and any research posing more than a minimal risk to the child subject must also directly benefit the child.⁷⁹

One area of stark contrast between the federal regulation of domestic research and foreign clinical trials is in the IND requirement. As currently written, federal law does not require sponsors conducting clinical research for an NDA abroad to obtain an IND before commencing trials.⁸⁰ Thus, a drug manufacturer can go forward with its three-phase trials without first giving the FDA an opportunity to review the trial’s design. Instead, the FDA will only evaluate the merits and framework of the study when the sponsor submits the data in order to obtain approval to market the drug in the U.S.⁸¹ While prospective review of foreign clinical trials would further burden the resource-strapped FDA,⁸² situations like Kano show the need for increased oversight of clinical trials in countries with ineffective human subject protections. As U.S. drug companies reap the benefits of these cheap drug trials, it is not unconscionable to require them to pay increased user fees to fund prospective FDA review of trial designs.

Prior to 2008, foreign trials had to adhere to the 1989 version of the Declaration of Helsinki or to alternate standards and guidelines if they would have provided better protection for human subjects.⁸³ However, in 2008 the FDA amended its regulations to abandon the Declaration of Helsinki standard in favor of requiring studies to adhere to “Good Clinical Practices” (“GCP”),⁸⁴ which are derived from the International Conference on Harmonization of Technical Requirements for Registra-

⁷⁷ 21 C.F.R. § 50.25; *see also* Cekola, *supra* note 13, at 135.

⁷⁸ 45 C.F.R. § 46.401. *See generally* COMMITTEE ON CLINICAL RES. INVOLVING CHILD., INST. OF MED. OF THE NAT’L ACAD., *ETHICAL CONDUCT OF CLINICAL RESEARCH INVOLVING CHILDREN* (Marilyn J. Field & Richard E. Behrman eds., 2004).

⁷⁹ *See* Ross, *supra* note 74, at 66. The National Commission for the Protections of Human Subjects “defined minimal risk as: the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical or psychological examination, of healthy children.” *Id.*

⁸⁰ 21 C.F.R. § 312.120(a).

⁸¹ *Id.*

⁸² *See generally* Food and Drug Admin., *FDA Science and Mission at Risk*, Remarks of Peter Barton Hutt, *available at* http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_02_FDA%20Report%20Appendices%20A-K.pdf (last visited Jan. 22, 2011).

⁸³ *HHS IG Report*, *supra* note 9, at 2.

⁸⁴ Carolyn R. Hathaway et al., *Looking Abroad: Clinical Drug Trials*, 63 *FOOD & DRUG L.J.* 673, 676-677 (2008).

tion of Pharmaceuticals for Human Use (ICH).⁸⁵ One of the primary criticisms of the Declaration of Helsinki was its relaxed requirements for informed consent when the subject receives medical care in conjunction with a clinical trial.⁸⁶ The GCPs purport to strengthen those informed consent requirements. In fact, unlike the Helsinki Declaration, the GCP requirements contain all the elements of 21 C.F.R. § 50.25,⁸⁷ which spells out the informed consent standards for domestic drug trials.

Nonetheless, while it appears the FDA has seemingly altered informed consent guidelines for human subjects in overseas trials, it is not clear why the agency has created this parallel track for research conducted mostly in the developing world. Instead of referring to GCPs, which were drafted by the ICH, an industry-sponsored,⁸⁸ consensus-driven initiative with no legal authority, the FDA should have amended its rules to directly apply the federal informed consent regulations from § 50.25 to foreign clinical research. The federal guidelines from § 50.25 have existed for decades and are ingrained in the research protocols of medical researchers conducting trials in the U.S. Applying the § 50.25 guidelines to *all* trials submitted to the FDA would incentivize drug manufacturers to treat foreign clinical subjects as they treat U.S. subjects, while removing the parallel informed consent process. After all, as the ICH guidelines are drafted by an industry-sponsored group, it is reasonable to fear that they could be diluted or amended without FDA participation.

Moreover, federal regulations do not require that an IRB oversee ongoing foreign clinical trials. Instead, the FDA requires sponsors seeking U.S. marketing approval to constitute an Independent Ethics Committee (IEC) to “review and approve” the study *before* commencement.⁸⁹ Unlike an IRB-monitored study,⁹⁰ there is no legal requirement that the IEC continually review the trial to ensure ethical and medical compliance. The FDA merely *suggests* that an IEC conduct yearly review of ongoing trials, but it is not mandated by law.⁹¹ Also, unlike IRBs, the FDA defines IECs very imprecisely as “review panel[s] that [are] responsible for ensuring the protection of the rights, safety, and well-being of

⁸⁵ Good Clinical Practice: Consolidated Guideline from International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 62 Fed. Reg. 25692 (May 9, 1997).

⁸⁶ Meier, *supra* note 58, at 523-27.

⁸⁷ Compare ICH Harmonized Tripartite Guideline: Guideline for Good Clinical Practice E6 (R1) (June 10, 1996), available at <http://www.ich.org/LOB/media/MEDIA482.pdf> [hereinafter *ICH Guideline*], with 21 C.F.R. §50.25 (2005).

⁸⁸ George J. Annas, *Globalized Clinical Trials and Informed Consent*, 360 No. 20 *NEW ENG. J. MED.* 2050, 2051 (2009).

⁸⁹ 21 C.F.R. § 312.120.

⁹⁰ See *INST. OF MED. OF THE NAT'L ACAD.*, *supra* note 78, at 97.

⁹¹ *FOOD AND DRUG ADMIN., GUIDANCE FOR INDUSTRY: E6 GOOD CLINICAL PRACTICE: CONSOLIDATED GUIDANCE*, available at <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM129515.pdf> (last visited Jan. 22, 2011).

human subjects involved in a clinical investigation.”⁹² While the FDA’s goal of ensuring that regulations are “sufficiently flexible to accommodate differences in how countries regulate the conduct of clinical research and obtain informed consent”⁹³ is laudable, this vague standard again creates another quasi-parallel standard for drugs tested in international settings. Although the FDA should be sensitive to the procedures of other countries’ regulatory bodies, the fact remains that many of the states where these trials occur have little to no effective protection for human subjects.⁹⁴ In fact, the Department of Health and Human Services’ (“HHS”) Inspector General has raised the concern “that FDA ‘receives minimal information on the performance of foreign institutional review boards . . . [and] has an inadequate database on the people and entities involved in foreign research.’”⁹⁵ And perhaps most disturbingly, the Inspector General concluded that the FDA “cannot necessarily depend on foreign investigators signing attestations that they will uphold human subject protections.”⁹⁶

Accordingly, the FDA should amend its regulations to mandate more specific and robust roles for these IECs as well as more agency oversight of the bodies, or require U.S.-based IRBs to monitor foreign clinical trials. While a U.S. IRB requirement could be criticized as regulatory imperialism, it is well within the FDA’s enabling statute to ensure safe and efficacious drugs through clinical oversight.⁹⁷ In order to prevent more Kano-type tragedies, Congress and the FDA should explore strengthening existing regulation regarding IECs and informed consent in foreign clinical trials. Without more oversight by the FDA, these quasi-parallel tracks for informed consent and approval, combined with lax or inadequate regulation in developing nations, will do nothing to increase protections for foreign clinical trial subjects.

A further area of concern in the regulation of foreign clinical research is the protection of child subjects.⁹⁸ Because most children in the developed world are relatively healthy compared to their counterparts in developing nations,⁹⁹ it is difficult for drug makers to find the requisite number of child subjects in the U.S. for trials of pediatric drugs and devices.¹⁰⁰ This shortage, combined with the “higher prevalence of many

⁹² *Id.* at 10; *cf. supra* note 76 (stating more specific guidelines).

⁹³ Food and Drug Admin. Notice, 7 Fed. Reg. 22, 800-01 (Apr. 28, 2008).

⁹⁴ Annas, *supra* note 88, at 2050-51.

⁹⁵ INST. OF MED. OF THE NAT’L ACAD., *supra* note 78, at 56.

⁹⁶ *Id.*

⁹⁷ *See generally* 21 U.S.C. §§ 301-99 (2005).

⁹⁸ INST. OF MED. OF THE NAT’L ACAD., *supra* note 78, at 57.

⁹⁹ *Id.*

¹⁰⁰ *Id.* As an example, in 2001, people under the age of 21 accounted for only about two percent of deaths and about 11 percent of hospital discharges in the U.S. *Id.*

serious medical problems in less developed countries,” incentivizes U.S. drug makers to look abroad for pediatric subjects.¹⁰¹ The incident in Kano, Nigeria provides a shocking illustration of this problem. Again, while U.S. drug makers are required to follow the industry-developed ICH standards, when it comes to foreign clinical research, the ICH guidance contains no mention of protections for children.¹⁰² Given the historical exploitation of children for medical research¹⁰³ and the incentives that western drug manufacturers have to conduct pediatric trials in places like Kano, Nigeria, the FDA should subject pediatric drugs tested abroad to the same regulations as those enforced domestically.

Another existing federal regulation designed to oversee foreign research is the FDA’s power to carry out spot checks on clinical tests conducted abroad. Under 21 C.F.R. § 312.120, the agency must “be able to validate the data from the study through an onsite inspection if the agency deems it necessary.”¹⁰⁴ To further this local inspection capability, the agency requires sponsors of foreign research to maintain their records for two years after an agency decision on the drug’s marketability.¹⁰⁵ While studies and data on the effects of this regulation are scarce, a 2008 GAO study on the FDA’s foreign drug inspection program elucidates the state of the FDA’s overseas onsite inspection as a whole. This report revealed that the implementation of any onsite inspection regime has proven somewhat ineffectual.¹⁰⁶ While the agency has begun to establish an electronic database to keep track of foreign research establishments, the system does not give an accurate picture of these facilities.¹⁰⁷ Also, the FDA has been unable to liaise with foreign regulatory bodies to allow

¹⁰¹ *Id.*

¹⁰² See generally *ICH Guideline*, *supra* note 87.

¹⁰³ Ross, *supra* note 74, at 12. In the early nineteenth century, Edward Jenner infected children residing in an almshouse with smallpox and cowpox. Glenn Cohen, *Therapeutic Orphans, Pediatric Victims? The Best Pharmaceuticals for Children Act and Existing Pediatric Human Subject Protection*, 58 *FOOD & DRUG L.J.* 661, 672 (2003). Closer to our own time, Alfred Hess conducted trials on children from the Hebrew Infant Asylum in New York because, he said, it allowed “conditions which are insisted on in considering the course of experimental infection among laboratory animals, but which can rarely be controlled in a study of infection in man.” Ross, *supra* note 74, at 12.

¹⁰⁴ 21 C.F.R. § 312.120a(1)(ii) (2008).

¹⁰⁵ Paul R. DeMuro & Andrea Jaeger-Lenz, *How to Conduct Clinical Trials in the EU and Eastern Europe: Overview and Comparison with the U.S. System*, 10 No. 5 *J. HEALTH CARE COMPLIANCE* 21, 26 (2008); 21 C.F.R. § 312.120d (2008).

¹⁰⁶ See generally U.S. GOV’T ACCOUNTABILITY OFFICE, *GAO-08-701T, DRUG SAFETY: PRELIMINARY FINDINGS SUGGEST RECENT FDA INITIATIVES HAVE POTENTIAL BUT DO NOT FULLY ADDRESS WEAKNESSES IN ITS FOREIGN DRUG INSPECTION PROGRAM* (2008), available at <http://www.gao.gov/new.items/d08701t.pdf> (last visited Jan. 22, 2011).

¹⁰⁷ *Id.* at 11-12.

the agency to gain an accurate picture of which foreign sites should command the most intensive oversight.¹⁰⁸ Finally, and perhaps most disturbingly, the FDA does not have a dedicated team of foreign inspectors on staff, nor does it maintain a sufficient system of translators for those staff that do scrutinize foreign clinical sites.¹⁰⁹ This staffing problem is endemic to the drug regulator over all of its functions, as the agency has faced a waning budget and an expanded role over the last decade.¹¹⁰ While the FDA has recently opened a high profile office in China, its physical presence on the ground in the developing world, where more and more drugs are tested, is still very limited.¹¹¹ Certainly government spending has been under increased public attack,¹¹² but giving the FDA more resources is crucial to increasing the protections of foreign clinical subjects through onsite inspection.

Some scholars have argued that the concept of extraterritoriality bars the FDA from regulating in the realm of foreign clinical research, barring explicit Congressional intent to allow for this regulation.¹¹³ Under this concept of extraterritoriality, U.S. courts presume that in passing legislation, Congress did not intend for American law to apply to behavior abroad.¹¹⁴ However, looking to the plain language of Congress' grant of rule making authority to the FDA, the agency has the core power to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner"¹¹⁵ and to "protect the public health by . . . [ensuring] human and veterinary drugs are safe and effective."¹¹⁶ Given

¹⁰⁸ *Id.*

¹⁰⁹ *Id.* at 10.

¹¹⁰ See generally Food and Drug Admin., FDA Science and Mission at Risk, Remarks of Peter Barton Hutt, available at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_02_FDA%20Report%20Appendices%20A-K.pdf (last visited Jan. 22, 2011).

¹¹¹ See FOOD AND DRUG ADMIN., OFFICE OF INTERNATIONAL PROGRAMS, <http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofInternationalPrograms/default.htm>. A canvas of this site revealed only two permanent FDA offices in the developing world: in India and China. *Id.* Africa, where the Kano studies occurred, does not have any permanent FDA presence. *Id.*

¹¹² See Robert J. Barro, Editorial, *Government Spending is No Free Lunch*, WALL ST. J., Jan. 22, 2009, at A17.

¹¹³ See William Dubois, New Drug Research, *The Extraterritorial Application of FDA Regulations, and the Need for International Cooperation*, 36 VAND. J. TRANSNAT'L L. 161, 172-73 (2003); Jonathan Turley, "When in Rome": *Multinational Misconduct and the Presumption Against Extraterritoriality*, 84 NW. U. L. REV. 598, 603-605 (1990).

¹¹⁴ *Blackmer v. United States*, 284 U.S. 421, 437 (1932); Turley, *supra* note 113, at 599.

¹¹⁵ 21 U.S.C. § 393(b)(1) (2010).

¹¹⁶ 21 U.S.C. § 393(b)(2)(B).

the clear nature of the statute, and the fact that the above regulations and proposed changes are science driven decisions based on the quality of evidence submitted to the FDA for a *domestic* marketing license, no extraterritoriality problems seem likely to arise.

As demonstrated above, the FDA's existing regulatory regime is broad and has begun to deal with the problems inherent in the use of foreign clinical data to obtain an NDA. However, these regulations have created a "quasi-parallel" track for the protection of human subjects in foreign trials. By strengthening the oversight of trials with more robust IRB-type bodies, harmonizing informed consent requirements for U.S. and foreign trials, requiring clinical trial protections for children and requiring prospective review of all drug trials, the U.S. can further the protections for the human subjects that have become so integral to Americans' health.

IV. STATUTORY CHANGES

A. *Legislative Creation of a Narrow Jurisdictional Statute*

At the core of the human subject protection deficit lays the inability of vulnerable foreign citizens injured by U.S. pharmaceutical makers to obtain justice. While the Second Circuit has allowed aggrieved foreign subjects to sue domestic drug makers, this decision likely overreaches the Supreme Court's ATS jurisprudence.¹¹⁷ Given the Supreme Court's "vigilant door keeping" regarding ATS claims and its hesitancy to expand the statute beyond a "narrow class of international norms,"¹¹⁸ legislative action would be more prudent to allow injured human subjects to seek compensation.

"As a moth is drawn to the light, so is a litigant drawn to the United States."¹¹⁹ While perhaps overstated, this quote does capture the point that creating any new jurisdictional statute for parties injured abroad would allow foreign litigants to pick the U.S. forum because of higher damage awards compared to other nations' courts.¹²⁰ Also, traditionally the province of foreign relations has been left to the executive branch, and allowing suits to proceed in U.S. courts for disputes arising out of transactions taking place entirely on foreign soil could interfere with the executive's discretion in foreign relations.¹²¹ Congressional action to

¹¹⁷ See *supra* notes 20-22 and accompanying text.

¹¹⁸ *Abdullahi v. Pfizer*, 562 F.3d 163, 192 (2d Cir. 2009) (Wesley, J., dissenting).

¹¹⁹ *Liaw Su Teng v. Skaarup Shipping Corp.*, 743 F.2d 1140, 1146 (5th Cir. 1984).

¹²⁰ See Russell J. Weintraub, *How Substantial is Our Need for a Judgments-Recognition Convention and What Should We Bargain Away to Get It?*, 24 *BROOK. J. INT'L L.* 167, 212 n.272 (1998-1999).

¹²¹ See Brief for Washington Legal Foundation as Amici Curiae Supporting Petitioners at 7, *Abdullahi v. Pfizer, Inc.*, 562 F.3d 163 (2009) (No. 09-34); see also *Ex Parte Republic of Peru*, 318 U.S. 578, 587 (1943) (opining that claims involving international relations and immunity usually left to State Department and President).

allow plaintiffs injured abroad by American pharmaceutical companies to sue in the U.S. could mitigate these concerns to some extent.

Regarding national forum shopping, in creating a functional expansion of the ATS, Congress would be able to limit the scope of lawsuits permitted in federal courts.¹²² Because myriad western pharmaceutical companies test drugs abroad,¹²³ expanding federal jurisdiction over these claims broadly could drain U.S. judicial resources. Instead, Congress should allow litigants allegedly injured only by U.S. pharmaceutical corporations, or foreign subsidiaries of U.S.-owned drug makers, to gain access to the federal courts. While any legislative jurisdictional changes in this sector are certain to encounter heavy lobbying by the politically powerful pharmaceutical industry,¹²⁴ it is more likely to give injured human subjects some access to compensation than the restrictive ATS. While it could be argued that litigants do have access to compensation through U.S. courts by suing in the Second Circuit, given the peculiar facts of *Abdullahi*, it is far from certain that future litigants could also bring an action.¹²⁵

Concerning the executive branch's discretion in foreign relations, Congressional action is a more effective way to ensure that this power is safeguarded. Here, the legislature, through consultation with and political pressure from executive officials, could tailor any jurisdictional measures to exclude litigants from countries where the judicial system is adequate. Further, Congress could except litigants from certain countries if the executive branch believes litigation would result in unacceptable diplomatic strains.

B. Behavioral Change

1. Existing Regulatory Sanctions

One possible explanation for the FDA's inability to change pharmaceutical companies' conduct in developing overseas studies is a lack of severe sanctions when researchers exploit foreign subjects.¹²⁶ Given the lack of clarity concerning the use of the existing Food, Drug and Cosmetic Act ("FDCA") to impose criminal sanctions on offending investigators, and the government's historic inability to change pharmaceutical companies'

¹²² See U.S. CONST. art. III, § 1.

¹²³ See Annas, *supra* note 88, at 2050.

¹²⁴ See Heidi Grygiel, *Now They GATT Worry: The Impact of the GATT on the American Generic Pharmaceutical Industry*, 6 U. BALT. INTELL. PROP. L.J. 47, 47 (1997) (noting the political power of the drug industry).

¹²⁵ Petition for Writ of Certiorari, *Abdullahi*, 562 U.S. 163 (09-34) (addressing opposing party's view of the unlikelihood of a reoccurrence due to the highly specific facts of the case).

¹²⁶ See Samantha Evans, *The Globalization of Drug Testing: Enforcing Informed Consent Through the Alien Tort Claims Act*, 19 TEMP. INT'L & COMP. L. J. 477, 505 (2005).

illegal behavior,¹²⁷ this note will propose fresh Congressional action to penalize the exploitation of foreign human subjects by researchers. In examining proposals for change in this realm, the Foreign Corrupt Practices Act, provides a useful parallel and model.

Under the Food, Drug and Cosmetic Act, there are multiple ways in which the FDA could proceed against drug makers who exploit clinical subjects abroad. Section 331, dealing with prohibited criminal acts under the FDCA, provides several possible avenues.¹²⁸ Under § 331(e), the FDA could proceed against researchers who did not provide access to their records concerning foreign clinical trials.¹²⁹ This section would not prove effective, however, in instances where the researchers may have simply covered up trial discrepancies, such as the alleged violations in *Abdullahi*.¹³⁰ Sections 331(y)(1) and 331(jj)(2) could address this shortfall, as they criminalize the submission of false reports to the FDA and the failure to submit clinical trial information.¹³¹ Despite these possibilities, a major shortcoming in the violations section of the FDCA is the lack of criminal sanctions for violations of informed consent. Certainly, without the proper informed consent procedure or documentation, a drug maker will simply not receive an NDA.¹³² However, given the FDA's limited ability to oversee foreign researchers, and whether they actually obtained the informed consent of the subjects, discussed *supra*, proper regulation in this realm is not possible. Also, actions against researchers and physicians for failing to obtain informed consent have traditionally been civil matters in the United States.¹³³ But as this note has discussed,¹³⁴ the ability of foreign subjects to access U.S. courts through existing jurisdictional mechanisms is doubtful.

¹²⁷ One need only look at the \$2.3 billion paid by Pfizer in January of 2009 to settle allegations of off-label drug promotion. Ron Winslow, *Pfizer Sets \$2.3 Billion Settlement*, WALL ST. J., Jan. 27, 2009, at B2. Earlier in January of 2009 Eli Lilly agreed to pay \$1.4 billion to settle similar allegations. *Id.*

¹²⁸ 21 U.S.C. § 331 (2005).

¹²⁹ The statute reads in relevant part:

The following [act] and the causing thereof are prohibited:

(e) The refusal to permit access to or copying of any record as required by section 350a, 350c, 350f(g), 350e, 354, 360bbb-3, 373, 374(a), 379aa, or 379aa-1 of this title; or the failure to establish or maintain any record, or make any report, required under section 350a, 350c(b), 350f 350e, 354, 355(i) or (k), 360b(a)(4)(C), 360b(j), (l), or (m), 360ccc-1(i), 360e(f), 360i, 360bbb-3, 379aa, 379aa-1, 387i, or 387t of this title or the refusal to permit access to or verification or copying of any such required record.

21 U.S.C. § 331e (2009).

¹³⁰ See *Abdullahi v. Pfizer, Inc.*, 562 F.3d 163 (2d Cir. 2009).

¹³¹ 21 U.S.C. §§ 331(y)(1), (jj)(2) (2009).

¹³² See 21 C.F.R. § 312.2.

¹³³ Margaret Z. Johns, *Informed Consent: Requiring Doctors to Disclose Off-label Prescriptions and Conflicts of Interest*, 58 HASTINGS L.J. 967, 1008 (2007).

¹³⁴ *Supra* Part I.

Despite the ability of the FDA to bring proceedings against offending trial sponsors for violations of the FDCA, as it now stands there is considerable confusion regarding whether individual clinical investigators who violate FDA regulations are subject to criminal sanctions.¹³⁵ In rejecting a petition for a writ of certiorari in *United States v. Palazzo*, the Supreme Court lost an opportunity to clear up this uncertainty.¹³⁶ This case, combined with two other similar cases spanning the past quarter century,¹³⁷ centered around the prohibited acts section¹³⁸ of the FDCA and the reporting requirements subsection of the FDCA's new drug section.¹³⁹ In these three cases, the courts grappled with the question of whether the FDCA's statutory language mandating reporting requirements for clinical trials only covered drug manufacturers, or also extended to the individual

¹³⁵ Aysha Somusandarum, *United States v. Palazzo: The Scope of Criminal Liability for Clinical Investigators*, 12 No. 1 J. HEALTH CARE COMPLIANCE 53, 53 (2010).

¹³⁶ *Id.*

¹³⁷ *United States v. Smith*, 740 F.2d 734, 737-38 (9th Cir. 1984); *United States v. Garfinkel*, 29 F.3d 451, 553-34 (8th Cir. 1994).

¹³⁸ 21 U.S.C. § 331 (2005). In relevant part, the statute reads:

The following acts and the causing thereof are prohibited:

(h) The giving of a guaranty or undertaking referred to in section 333(c)(2) of this title, which guaranty or undertaking is false, except by a person who relied upon a guaranty or undertaking to the same effect signed by, and containing the name and address of, the person residing in the United States from whom he received in good faith the food, drug, device, tobacco product, or cosmetic; or the giving of a guaranty or undertaking referred to in section 333(c)(3) of this title, which guaranty or undertaking is false.

.....

(y) In the case of a drug, device, or food-

(1) the submission of a report or recommendation by a person accredited under section 360m of this title that is false or misleading in any material respect. . . .

.....

(jj)(1) The failure to submit the certification required by section 282(j)(5)(B) of Title 42, or knowingly submitting a false certification under such section.

¹³⁹ 21 U.S.C. § 355 (2009). In relevant part, the statute reads:

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon-

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing

investigators conducting the study.¹⁴⁰ While the Ninth Circuit did not extend the statute's power to individual investigators,¹⁴¹ the Fifth and Eighth Circuits ruled that the FDCA covered individual researchers.¹⁴² In reaching these different conclusions, the three courts applied the *Chevron* doctrine to determine whether Congress had spoken directly to the subject of regulation and whether the agency acted reasonably in the absence of clear congressional guidance.¹⁴³

None of the courts above were dealing with investigators or drug makers who failed to conform to informed consent or investigation oversight laws in foreign trials.¹⁴⁴ Nevertheless, this circuit split illuminates the difficulties inherent in changing the behavior of drug makers and researchers through the existing FDCA. Should the FDA utilize existing law or its rule making authority to impose harsher sanctions on investigators and manufacturers testing abroad, the agency could become involved in challenges to its authority in federal court. In light of the confusion over agency-imposed criminal sanctions on individuals and the judiciary's recent trend of decreased deference towards the FDA,¹⁴⁵ congressional action is necessary to protect foreign clinical subjects.

2. A Foreign Corruption Parallel for Foreign Trial Sponsors¹⁴⁶

In the late 1970s post-Watergate fallout, Congress uncovered a host of bribes given to domestic political campaigns.¹⁴⁷ After initial allegations, federal law enforcement and regulatory investigations also uncovered U.S. corporate payments to foreign regimes to win lucrative contracts and preferable business arrangements.¹⁴⁸ Congress passed the Foreign Corrupt Practices Act ("FCPA") in response.¹⁴⁹

¹⁴⁰ Somusandarum, *supra* note 135, at 53-56, 70-71.

¹⁴¹ United States v. Smith, 740 F.2d 734 (9th Cir. 1984).

¹⁴² United States v. Palazzo, 558 F.3d 400 (5th Cir. 2009); United States v. Garfinkel, 29 F.3d 451 (8th Cir. 1994).

¹⁴³ Somusandarum, *supra* note 135, at 54.

¹⁴⁴ See generally United States v. Smith, 740 F.2d at 734; United States v. Garfinkel, 29 F.3d at 451; United States v. Palazzo, 558 F.3d at 400.

¹⁴⁵ See James T. O'Reilly, *Losing Deference in the FDA's Second Century: Judicial Review, Politics, and a Diminished Legacy of Expertise*, 93 CORNELL L. REV. 939, 973-76 (2008) (tracing the path of judicial deference of FDA regulations and decisions).

¹⁴⁶ In 2010, the Department of Justice began investigating whether drug makers had violated the actual Foreign Corrupt Practices Act to boost sales and approvals, an interesting issue beyond the scope of this note. Michael Rothfeld, *Drug Firms Face Bribery Probe*, WALL ST. J., Oct. 22, 2010, at B1.

¹⁴⁷ See generally Oliver J. Armas, *The U.S. Foreign Corrupt Practices Act: An Overview*, 22 SPRING INT'L L. PRACTICUM 31 (2009).

¹⁴⁸ *Id.*

¹⁴⁹ *Id.* The statute reads in relevant part:

It shall be unlawful for any issuer which has a class of securities registered pursuant to section 78l of this title or which is required to file reports under

Broadly speaking, the FCPA makes it a criminal offense for any U.S. issuer of securities, person, or foreign person present in the U.S. to make a corrupt payment to an overseas official, political party, or candidate for the purpose of “obtaining or retaining business.”¹⁵⁰ Also, the FCPA consists of both criminal and civil sanctions, with civil enforcement authority falling on the Securities & Exchange Commission and the Attorney Gen-

section 78o(d) of this title, or for any officer, director, employee, or agent of such issuer or any stockholder thereof acting on behalf of such issuer, to make use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay, or authorization of the payment of any money, or offer, gift, promise to give, or authorization of the giving of anything of value to-

- (1) any foreign official for purposes of-
 - (A)(i) influencing any act or decision of such foreign official in his official capacity, (ii) inducing such foreign official to do or omit to do any act in violation of the lawful duty of such official, or (iii) securing any improper advantage; or
 - (B) inducing such foreign official to use his influence with a foreign government or instrumentality thereof to affect or influence any act or decision of such government or instrumentality, in order to assist such issuer in obtaining or retaining business for or with, or directing business to, any person;
- (2) any foreign political party or official thereof or any candidate for foreign political office for purposes of-
 - (A)(i) influencing any act or decision of such party, official, or candidate in its or his official capacity, (ii) inducing such party, official, or candidate to do or omit to do an act in violation of the lawful duty of such party, official, or candidate, or (iii) securing any improper advantage; or
 - (B) inducing such party, official, or candidate to use its or his influence with a foreign government or instrumentality thereof to affect or influence any act or decision of such government or instrumentality in order to assist such issuer in obtaining or retaining business for or with, or directing business to, any person; or
- (3) any person, while knowing that all or a portion of such money or thing of value will be offered, given, or promised, directly or indirectly, to any foreign official, to any foreign political party or official thereof, or to any candidate for foreign political office, for purposes of-
 - (A)(i) influencing any act or decision of such foreign official, political party, party official, or candidate in his or its official capacity, (ii) inducing such foreign official, political party, party official, or candidate to do or omit to do any act in violation of the lawful duty of such foreign official, political party, party official, or candidate, or (iii) securing any improper advantage; or
 - (B) inducing such foreign official, political party, party official, or candidate to use his or its influence with a foreign government or instrumentality thereof to affect or influence any act or decision of such government or instrumentality, in order to assist such issuer in obtaining or retaining business for or with, or directing business to, any person.

15 U.S.C. § 78dd-1 (1998).

¹⁵⁰ *Id.*; Armas, *supra* note 147, at 31.

eral.¹⁵¹ Finally, foreign-owned subsidiaries of U.S. corporations as well as foreign citizens acting for these corporations and U.S. citizens acting in violation of the statute on behalf of foreign companies are subject to the FCPA.¹⁵²

Given the increased use of foreign trials by U.S. pharmaceutical companies, the poor regulatory structures of the countries that host these tests,¹⁵³ and the possible inability of the FDA to sanction trial sponsors for violating existing regulations,¹⁵⁴ Congress should enact a mechanism of criminal sanctions similar to the FCPA to deter human subject abuses. Like the FCPA's tailored scope, any criminal legislation aimed at clinical trial sponsors should be customized to encompass both corporate sponsors of clinical trials as well as individual researchers. This individual mandate is important, as the community of individual pharmaceutical researchers is not large.¹⁵⁵ Unlike the massive number of individuals who could conceivably be prosecuted under the FCPA, the prosecution of an individual researcher would immediately command this small community's attention. Also, given the difficult nature of deterring pharmaceutical company malfeasance,¹⁵⁶ any legislative change seeking to deter corporate persons should reach beyond the companies' general treasury. Rather than solely seeking financial penalties against corporations as a whole, which often lead to non-prosecution agreements or deferred prosecution agreements under the FCPA,¹⁵⁷ Congress should seek to deter foreign human subject abuses by imposing direct sanctions on individual board members at particularly egregious violators. This type of extraordinary sanction could take the form of a similar tax code provision that inflicts liability on non-profit board members who make decisions favoring insiders.¹⁵⁸

As with the FCPA, a foreign drug trial statute should threaten civil sanctions as well as criminal liability. In seeking to deter researchers, Congress should empower HHS to exclude individual doctors who participate in violative foreign clinical trials from taking part in any projects that receive Medicare or other federal funding. Also, just like HHS's

¹⁵¹ U.S. DEP'T OF JUSTICE, FOREIGN CORRUPT PRACTICES ACT: ANTIBRIBERY PROVISIONS; LAY-PERSON'S GUIDE, <http://www.justice.gov/criminal/fraud/fcpa/docs/lay-persons-guide.pdf> (last visited Jan. 23, 2011).

¹⁵² Armas, *supra* note 147, at 31.

¹⁵³ See Wollensack, *supra* note 7, at 748.

¹⁵⁴ See *supra* Part II.B.

¹⁵⁵ In its 2001 report, the HHS Inspector General reported about 4,000 U.S. researchers abroad. HHS IG Report, *supra* note 9, at 6.

¹⁵⁶ See Winslow, *supra* note 127, at B2 (reporting on the billion dollar unsuccessful attempt to change off-label promotion).

¹⁵⁷ David C. Weiss, *The Foreign Corrupt Practices Act, SEC Disgorgement of Profits, and the Evolving International Bribery Regime: Weighing Proportionality, Retribution, and Deterrence*, 30 MICH. J. INT'L L. 471, 482 (2009).

¹⁵⁸ 26 U.S.C. § 4958 (2005).

existing power to exclude companies who violate Medicare regulations from the program,¹⁵⁹ the FDA should be able to exclude, for a limited time, an individual or company found to have violated FDA regulations from participating in any trial seeking an NDA. Given the “small number of mammoth companies” that comprise the global pharmaceutical industry,¹⁶⁰ the stakes would be disastrous for a major pharmaceutical company if the FDA barred their participation, if even for a short time.

While the above proposals are not exhaustive or exacting, they would serve as a foundation to put more authority into the existing federal structure of human subject protection. A panoply of criminal and civil sanctions drafted by Congress would provide protections to foreign subjects before they are injured, and would also serve to avoid the judicial ambiguities that plague the sanctions under current law.

V. CONCLUSION

This note has discussed the perils facing foreign human subjects in foreign clinical trials. These dangers are exacerbated by the difficulty for aggrieved foreign human subjects to obtain justice at home or in a U.S. courtroom. The problem is complex but not indomitable. Through regulatory and statutory changes that allow for, among other things, more robust oversight of foreign trials, a limited jurisdictional statute for foreign trials and the criminalization of foreign human subject abuse, the U.S. can begin to arrest a flawed system that produces blockbuster drugs by exploiting some of the world’s most vulnerable populations. This nuanced problem will not be resolved quickly or without difficulty, but policy makers and stakeholders must change their behavior in order to avoid future Kano horrors.

¹⁵⁹ 42 U.S.C. §1320a-7 (2005).

¹⁶⁰ Finnuala Kelleher, *The Pharmaceutical Industry’s Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations*, 38 *COLUM. J.L. & SOC. PROBS.* 67, 94 (2004).