

The Human Factor:

Globalizing Ethical Standards in Drug Trials Through Market Exclusion

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- I. Introduction (2)**
- II. Exorcising History’s Demons—The Genesis of Current Ethical Norms (4)**
 - A. Nuremberg Code—Reacting to Nazi Horrors (4)**
 - B. Declaration of Helsinki—Tempering the Nuremberg Code (8)**
 - C. The Belmont Report: Awakening to American Abuses (9)**
 - D. Applicability of Ethical Guidelines to Globalized Trials (13)**
 - 1. FDA Regulations and the Declaration of Helsinki (13)**
 - 2. Umbrella of International Ethical Guidelines (15)**
 - 3. International Ethical Guidelines Without an “International” Effect (17)**
- III. The Body Trade—The Globalization of Human Clinical Research (18)**
 - A. Drugs, Drugs, Everywhere, Nor Any Drop of Profit? (18)**
 - B. Severing the Umbilical Cord with Academic Institutions (20)**
 - C. Exhuming Conrad? Pfizer’s Excursion into the Heart of an Epidemic (23)**
 - 1. Medical Crisis in Nigeria (23)**
 - 2. Kano, A Tale of Two Camps (24)**
 - 3. The Unraveling of Trovan (26)**
- IV. Using Soft Law to Play Hard Ball With The Drug Industry (28)**
 - A. The Challenge of Regulating Multinational Corporations (28)**
 - B. Is the Alien Tort Statute a Viable Solution for Enforcing International Violations of Ethical Standards? (30)**
 - C. Is International Enforcement of Ethical Standards Feasible? (35)**
 - D. Using Soft Law to Exploit Hard Regulations That Have International Effects (38)**
 - E. Applying Proposal to the Trovan Case (41)**
- V. Conclusion (44)**

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I. Introduction

She was only ten years old and suffering from a serious infectious disease that was sweeping through West Africa, bacterial meningitis.¹ Meningitis attacks the protective membranes covering the brain and spinal cord and can cause for serious neurologic damage or even death.² The good news for this girl's family was that there is an effective treatment for this disease, intravenous antibiotics.³ Further, once they arrived at the clinic in Kano, Nigeria, they saw Western doctors in white coats offering to provide drugs for free.⁴ However, three days later the girl died, not having received any proven antibiotic therapy, but only an experimental drug called Trovan.⁵ The family of the girl later claimed, along with many others, that instead of receiving medical care, they were unwitting participants in a multinational drug company's experimental trial that led to the deaths or serious impairment of many children.⁶ Why would a drug company ever do something like this? Well, if data from the experiment helped the drug obtain market approval and it became a blockbuster, this company would have over a billion reasons to do this.⁷

Given the promise of tremendous financial reward a blockbuster therapy might generate, there is a strong incentive to move drug research and development to

¹ Joe Stephens, *The Body Hunters: Exporting Human Experiments: Where Profits and Lives Hang in the 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 (the Washington Post published a six-part series examining the growing phenomenon of international clinical drug testing, highlighting that the system tends to exploit the poor and uneducated while betraying promises of safety and effectiveness to patients and consumers).

² World Health Organization: Meningococcal Meningitis, accessed at <http://www.who.int/mediacentre/factsheets/fs141/en/>.

³ See Stephens *supra* note 1.

⁴ *Id.*

⁵ *Id.*

⁶ *Abdullahi v. Pfizer*, 2002 U.S. Dist. LEXIS 17436.

⁷ Trovan was projected by some Wall Street analysts to be a \$1 billion drug, *see* Stephens *supra* note 1.

“developing countries” with minimal ethical guidelines and little transparency.⁸ The danger in this “race for the prize (bottom)” is the exploitation of subaltern populations who have little legal recourse to hold drug companies accountable for the harm they suffer as a result of unethical clinical trials.⁹ In other words, the drug industry is acutely aware that there is minimal threat of costly civil and criminal legal sanctions for any of their ethical violations in impoverished countries. The result is that the relaxing of international norms of ethics for drug trials in developing countries has become an industry practice.¹⁰ This does not mean that drug companies are inherently “unethical” institutions—these corporations are made of people who are simply being human and responding to the structural incentives that exist. Likewise, we need to recognize that the statistical numbers reported in these clinical trials in developing nations are actual human individuals, who are also responding to the structural incentives that exist for them, no promise of health care unless they submit to risky experiments.

This article is part one of a two-part series that seeks to deter unethical clinical drug trials in developing nations by preventing products developed unethically from

⁸ The term “developing countries” is used here to denote countries with a relatively low standard of living, undeveloped infrastructure, and low human development index score. This term has largely replaced the use of “third world” to describe similarly situated nations.

⁹ The term subaltern is used here in the Gramscian sense to denote marginalized individuals or groups that does not possess agency as a consequence of their social status. See Antonio Gramsci, *Selections from the Prison Notebooks of Antonio Gramsci* 52-55 (Quintin Hoare & Geoffrey Nowell Smith eds. & trans., 1971).

¹⁰ See David M. Kent et al., *Clinical Trials in Sub-Saharan Africa and Established Standards of Care: Systematic Review of HIV, Tuberculosis, and Malaria Trials*, 292 JAMA 237, 239 (2004) (study looking at compliance with Declaration of Helsinki’s “best proven” therapeutic standard found that only 16% of studies met this standard despite 81% of these studies reporting oversight by an ethics review board). See also *Abdullahi v. Pfizer*. These facts are alleged by plaintiffs in this case and have been corroborated by independent witnesses in a variety of press accounts and legal journal articles. See Stephens *supra* note 1. See also, Sarah Bosely, *New Drug “Illegally Tested on Children”: Pfizer Accused of Irregularities During Clinical Trial in Nigeria*, THE GUARDIAN (LONDON), Jan. 17, 2001, at 19.

gaining market approval.¹¹ In particular, this article argues for a combination of “soft-law” techniques including more robust and subaltern-centric surveillance of international drug trials to enforce existing “hard law” rules within the regulatory agencies of the United States and European Union that require clinical drug research to adhere to international ethical standards. The intended result is to create a stiff economic penalty, exclusion from lucrative markets for unethical testing practices. This in turn will create a strong ex ante economic incentive for drug companies to conduct drug trials ethically.¹²

First, this article will first outline how our current medical ethics regime has emerged as a reaction to historical ethical abuses. Next, this article will address how globalization has transformed human drug testing trials, and in the process rendered inadequate the current ethics regime which does not operate well across international borders into developing nations.¹³ Lastly, this article will describe how soft law, which can work effectively across international borders, can be used to effectuate hard law sanctions of blocking market approval within the United States (U.S.) and European Union (E.U.) to deter unethical practices in clinical drug trials.

II. Exorcising History’s Demons—The Genesis of Current Ethical Norms

¹¹ Part Two of this paper proposes stripping intellectual property rights for drugs that are developed unethically not only to serve as an additional deterrent, but to address the social cost issue that arises if a medically beneficial drug is excluded from the market.

¹² In a sense, this proposal operates almost like the “fruit of the poisonous tree” doctrine from U.S. jurisprudence. This doctrine describes evidence obtained with the help of information gathered illegally. The logic of this term is that if the source of the evidence (“tree”) is tainted, then anything gained from the tree (“fruit”) is likewise tainted. To remove the incentive for illegal searches and ultimately deter such behavior, the tainted information is generally excluded, or not admissible in court.

¹³ See Kent *supra* note 5. See also *Abdullahi v. Pfizer, Inc.* (Trovan Case), No. 01 Civ. 8118, 2005 WL 1870811 (S.D.N.Y. Aug. 9, 2005) (class-action plaintiffs case was dismissed on both grounds of failure to state a claim under the Alien Tort Statute and *forum non conveniens*).

This section will describe how the development of international bioethical guidelines has largely been a narrative of society reacting to medical and scientific transgressions after the fact. In particular, this section will describe three of the most prominent statements of bioethics: the Nuremberg Code, the World Medical Association's (WMA) Declaration of Helsinki, and the U.S.'s Belmont Report. Then, this section will describe how these ethical standards are applied by drug regulatory agencies to human clinical trials.

A. Nuremberg Code—Reacting to Nazi Horrors

Modern bioethics, in the form of the Nuremberg Code, arose as a strong reaction against the horrific Nazi medical experiments during World War II. The sheer inhumanity of these experiments became public record during the Nuremberg Trials held immediately after World War II.¹⁴ These experiments were invariably performed on prisoners in concentration camps and not volunteers affiliated with the German military or Nazi party. The purported rationales for these experiments ranged from the advancement of medical and military knowledge to proving pseudo-scientific racist theories. In one of the “military” experiments, Dr. Sigmund Rascher placed prisoners in a decompression chamber to determine the best means of rescuing pilots who had to abandon their planes at high altitudes where there was little oxygen and low atmospheric

¹⁴ The Japanese military tested biowarfare agents on unwitting Chinese subjects in occupied Manchuria including spraying infectious diseases by airplane over populated areas and infecting well-water and other foodstuffs and then examining the rate of disease and effect on the Chinese population. Unlike with the Nazi experiments, no international war crimes tribunal was held for these Japanese experiments. The reason is that the U.S. military was interested in the results of the Japanese experiments for their own biowarfare program and granted the Japanese scientists immunity in exchange for sharing their research findings. See Sharona Hoffman, *Beneficial and Unusual Punishment: An Argument in Support of Prisoner Participation in Clinical Trials*, 33 *Ind. L. Rev.* 475, at 483.

pressure.¹⁵ Rascher would often dissect victims' brains, some while still alive, to show that high altitude sickness was caused by the formation of tiny air bubbles in the blood vessels in a particular part of the brain. In another trial, to discover how long downed German pilots could survive in the frigid North Sea, Rascher immersed prisoners in ice water tanks for varying amounts of time and then attempted to revive them using different warming methods.¹⁶ Naturally, many of these prisoners died of hypothermia. Other Nazi trials subjected prisoners to the effects of sea water, mustard gas, bone transplantation, sterilization, and various infectious diseases. At the conclusion of the Nuremberg trials, twenty three Nazi doctors were convicted of committing “war crimes and crimes against humanity” and seven of them were executed for their actions.¹⁷

The lasting legacy of this tribunal is the Nuremberg Code (“Code”), which set out for the first time an international consensus statement of what constituted ethical treatment of humans in clinical trials. The Code contains ten points that elucidate under what circumstances medical experimentation on humans is ethical and permissible.¹⁸ The

¹⁵ See Nuremberg Medical Trials Project—Medical Trial Transcript December 11, 1946, at 207-209, accessed at http://nuremberg.law.harvard.edu/NurTranscript/TranscriptPages/248_209.html.

¹⁶ See *Id.* at 231.

¹⁷ See Hoffman, *supra* note 9, at 483.

¹⁸ The Ten Points of the Nuremberg Code are:

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

first line of the Code states, “The voluntary consent of the human subject is absolutely essential.”¹⁹ However, the essential core of the Code is that testing on human subjects can only be done if *voluntary* and *informed* consent is received from test participants. In other words, human subjects cannot be coerced into participating in experiments or be kept ignorant of the risks to which they are being exposed.

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2. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
 3. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
 4. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
 5. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
 5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
 6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
 7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
 8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
 9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
 10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject. *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* Washington, D.C.: U.S. Government Printing Office, 1949.

¹⁹*See Id.*

B. Declaration of Helsinki—Tempering the Nuremberg Code

The World Medical Association (WMA), often confused with the United Nation's World Health Organization (WHO), describes itself as an "apolitical" organization that "has (and indeed seeks to have) no actual powers, yet the Declarations and Statements it has made over the years have carried great weight in national and international debates."²⁰ Indeed, the WMA's Declaration of Helsinki (Declaration) has been described as "the fundamental document in the field of ethics in biomedical research."²¹ In the years following the issuance of the Nuremberg Code, many medical researchers complained that its absolutist stance on informed consent was archaic and "a product of and reaction to Nazi terror . . . no longer useful for today's researchers."²² Further, the Code only focused on nontherapeutic research, and did not focus on the broad field of therapeutic research where there is some promise of benefit to the subjects (e.g., an experimental cancer drug shown to be effective in animals).

Drafted in 1964, the Declaration set forth "a list of duties and responsibilities that are expected of all physicians taking part in experimental research on humans."²³ Implicitly recognizing the Code as the ur text of bioethics, the Declaration addressed researchers' criticisms by not requiring consent for therapeutic research "where the researcher believes that it is unnecessary or difficult to obtain" and allowing for proxy

²⁰ Parenthetical in original. See World Medical Association policy statement accessed at www.wma.net/e/policy/index.htm

²¹ See Lori Alvino, *Who's Watching the Watchdogs? Responding to the Erosion of Research Ethics by Enforcing Promises*, 103 COLUM. L. REV. 893, 897 (2003).

²² See William Dubois, *New Drug Research, The Extraterritorial Application of FDA Regulations, and the Need for International Cooperation*, 36 VAND. J. TRANSNAT'L LAW 161, 203 (2003).

²³ See David Carr, *Pfizer's Epidemic: A Need for International Regulation of Human Experimentation in Developing Countries*, 35 CASE W. RES. J. INT'L L. 15, 23 (2003).

consent such as through a legal guardian or a community leader.²⁴ However, with the exception to consent requirements, the Declaration generally followed the contours laid out by the Code and its stated purpose was to have medical researchers put “their patients interest first.”²⁵

C. The Belmont Report: Awakening to American Abuses

The publicized horrors of Nazi experiments being performed on people with no agency led to a profound rethinking of scientific research that involved human subjects. Following World War II, almost no country has sanctioned the use of prisoners in clinical trials with one major exception—the United States.²⁶ Indeed the United States has a long history of conducting clinical trials on prisoners that preceded and continued long after the Nuremberg Trials. In fact, during the Nuremberg Trials, defense attorneys futilely argued that the Nazi physicians’ actions were tantamount to “the wartime experiments in the United States such as those carried out at the Joliet, Illinois, prison in which treatments for malaria were sought by physicians who had to first infect the volunteer prisoners with the disease.”²⁷ The U.S. military also experimented on prisoners for research that involved dengue fever, sleeping sickness, and sand-fly fever.²⁸ Further, the U.S. military and CIA has a long history of testing psychoactive drugs on enlisted

²⁴ See Finnuala Kelleher, *The Pharmaceutical Industry’s Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations*, 38 COLUM. J.L. & SOC. PROBS. 67, 74 (2004).

²⁵ See WMA policy statement, *supra* note 15.

²⁶ Members of the dissident Chinese group, Falun Gong, have repeatedly alleged that the Chinese government has performed organ harvesting procedures on some of their imprisoned members. The Chinese government denies these allegations but has a less than stellar human rights record. See *China Harvesting Falun Gong Organs, Report Alleges*, CBC NEWS, July 6, 2006, accessed at <http://www.cbc.ca/canada/story/2006/07/06/china-falungong.html>.

²⁷ See Hoffman at 483. This argument failed as the prosecution pressed that the Nazi victims had no choice as to whether to participate in the experiments and the U.S. prisoners “volunteered to participate in clinical trials.” *Id.* Clearly the circumstances facing Nazi concentration camp prisoners and U.S. prisoners during War II are incomparable, but one can certainly question whether U.S. prisoners had adequate agency to genuinely “volunteer” for the trials.

²⁸ *Id.*

soldiers without informing subjects about what they were being tested with.²⁹ Following World War II, it was not the military, but rather the pharmaceutical industry that conducted most of the clinical trials involving prisoners. In fact, by 1969, 85% of new drugs were being tested on prisoners in over forty prison research facilities across the U.S.³⁰

However, the most infamous breach of medical ethics in the U.S. is probably the Tuskegee Syphilis Study, notorious for its audacity, scope, and persistence well past the Civil Rights Era.³¹ This study was conducted between 1932 and 1972 on hundreds of impoverished African American men who were promised free medical care for participating in the trial. After penicillin was proven to be an effective treatment for syphilis in 1947, the researchers logically had no justifiable reason to continue this trial. However, the Tuskegee researchers received federal approval to amend and continue their study by willfully denying treatment to their subjects so they could observe the natural course of untreated syphilis.³²

During the latter half of the twentieth century, certain other medical trials stand out for their brazen disregard of the human subjects involved. In the 1960s at

²⁹ See *Stanley v. CIA*, 639 F.2d 1146, 1149-53 (5th Cir. 1981) (court held that sovereign immunity barred plaintiff's claim that U.S. officials repeatedly gave him LSD, without his knowledge, while he was in the military; LSD was allegedly being tested as a "truth serum" intended for use during military interrogations). Several terrorism suspects that were held in Guantanamo Bay ("Gitmo") have alleged being "medically experimented" on by the U.S. military medical personnel, perhaps demonstrating that the lessons of the Nuremberg Doctors' Trial have been forgotten. See Laurie Bretton, *Frenchmen Say Guantanamo Detention Was Like Hell*, REUTERS, July 30, 2004; Robert Lifton, *Doctors and Torture*, 351 NEJM 415-416 (2004).

³⁰ See Hoffman at 475.

³¹ The Civil Rights Era is generally recognized as occurring from the mid 1950's to mid 1960's. See generally, Juan Williams, *Eyes on the Prize: America's Civil Rights Years, 1954-1965*. New York: Penguin Books, 1987. The post-Civil Rights political and social struggle by African-American groups during the 1970s has sometimes been characterized as the "Black Power Movement."

³² Even the flimsy rationale of scientific curiosity is hard to accept as a justification since the natural course of syphilis was well-known throughout history. Philosopher Frederic Nietzsche, artist Vincent Van Gogh, and composer Ludwig Van Beethoven have famously been alleged to have suffered from the end-stages of syphilis.

Willowbrook State Hospital, a New York State facility for “mentally defective children,” researchers studied hepatitis by deliberately infecting mentally retarded children with the hepatitis virus.³³ The children were either fed extracts of stool from infected children or directly injected with the virus. While this study was ongoing, Willowbrook Hospital stopped accepting new residents due to overcrowding. However, since the hepatitis program was granted its own space in the facility, it still had capacity to admit new patients. Therefore, in some instances parents were not allowed to admit their children to the hospital unless they “consented” to let their child participate in the study. In another notorious experiment that occurred in New York during the 1960s, researchers at Brooklyn Jewish Chronic Disease hospital injected live cancer cells into senile patients to observe their immunological responses

Taken as a whole the U.S. prison, Tuskegee, Willowbrook and Brooklyn Jewish trials all share certain characteristics. First, the experimental subjects or their guardians were never properly informed of the risks of being in the experiment. Second, the research did not promise any therapeutic benefit to the subjects. Third, and most tellingly, the social or physical status of the subjects identified themselves to medical researchers as having not having the same agency as fully empowered U.S. adults.

Therefore, these subjects could be exploited for the sake of scientific progress with little

³³ Experimentation on mentally challenged children has a long and troubling history in the U.S. During the 1940s and ‘50s, the Massachusetts Institute of Technology (MIT) and Quaker Oats fed radioactive iron to boys classified as “mentally retarded” to measure the effect of a cereal-heavy diet on mineral absorption. The boys, aged twelve to seventeen, were duped into thinking they were joining a “science club.” In addition to radioactive materials, “club members” were treated with extra portions of milk and trips to baseball games and the beach. Parents of the boys were not told the study involved radioactive materials nor that there would be any risks. MIT and Quaker Oats agreed to pay victims of this experiment \$1.85 million in 1997. See *MIT, Quaker Oats to Settle Radiation Experiment Suit*, CNN, December 31, 1997, accessed at <http://www.cnn.com/US/9712/31/radioactive.oatmeal/>.

worry that the subjects had enough power to hold researchers accountable for practices that the researchers undoubtedly would not consent to.³⁴

Public outrage over the Tuskegee trial coupled with the general social tumult of the early seventies forced Congress to take a stronger role in overseeing human clinical trials in the U.S. In 1974, Congress passed the National Research Act and pursuant to this Act the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Commission) was established. Increased scrutiny of prison testing facilities revealed evidence of coercion, lack of knowing consent, and unreported adverse health outcomes. As a consequence, in 1976, the Commission recommended a federal moratorium on funding and approving studies using prisoners until research criteria that protected the interests of prisoners could be drafted.³⁵ In 1979, building upon international consensus statements of bioethical principles, the Nuremberg Code and the Declaration of Helsinki, the Commission issued the Belmont Report as the U.S. federal government's official policy statement regarding research with human subjects.³⁶

³⁴ One provision of the Nuremberg Code holds that certain risky experiments are allowable if the researchers subject themselves to the same risks as the subjects. This type of provision is not reproduced in the Belmont Report or the Declaration of Helsinki, but clearly demonstrates the concern of the Nuremberg Code authors that researchers and subjects usually occupy different strata of power and that perhaps one check on abuse of such power differential is requiring that researchers be willing to subject themselves to the same risk as their subjects. *See* Nuremberg Code, *supra* note 13.

³⁵ *See* Hoffman at 488. The National Commission's recommendations including setting up Institutional Review Boards (IRB) for prison experiments. The use of inmates raised concerns not present when research subjects come from the general public. For instance, the IRB had safeguard that the advantages inmates received through participation in the trial with respect to food, recreation, living conditions, and monetary compensation, was not so great to render a prisoner incapable of balancing the risks and benefits of the trial. Further, the risks from the trial must be equivalent to those acceptable to non-incarcerated research subjects and participation in research trials could not be considered when making parole decisions. *Id.*

³⁶ The Belmont Report, 44. Fed Reg. 23 (Apr. 18, 1979). *See* Alvino at 895, "The federal regulations that currently govern federally funded research involving human subjects have their origins in two international codes: the Nuremberg Code and the Declaration of Helsinki.

The core principles of the Belmont Report are: respect for persons, beneficence, and justice.³⁷ The respect for persons principle reinforces the concept of informed consent requiring that “subjects enter into research voluntarily and with adequate information.” Under this principle, special scrutiny is applied in protecting those with diminished autonomy such as children, the mentally handicapped, or prisoners. The principle of beneficence requires that the potential risks to research subjects be balanced against the potential benefits to society and that research any study can only proceed if benefits outweigh the risks. The principle of justice requires fairness in the distribution of research benefits and burdens among differing populations. Thus, this principle prevents one group from bearing all of the risks and none of the benefits from research while another group receives all of the benefit but none of the risk.³⁸

Pursuant to the National Research Act, the Department of Health and Human Services (DHHS) instituted regulations governing human research that became known as the “Common Rule.” The Common Rule requires that all institutions receiving federal funds for a research using human subjects must establish Institutional Review Boards (IRBs) to oversee all human research and ensure compliance with DHHS regulations. Thus, it is primarily IRBs that implement the principles of the Belmont Report.

D. Applicability of Ethical Guidelines to Globalized Trials

1. FDA Regulations and the Declaration of Helsinki

³⁷ *Id.*

³⁸ As will be discussed in latter sections of this article, this justice principle is clearly being violated in many of the drug trials occurring in developing nations as the groups taking all of the risks are not the intended market for drug makers and likely cannot afford new drugs with patent protection.

The globalization of clinical trials really became enabled after a 1980 Food and Drug Administration (FDA) ruling that allowed data from foreign trials to be used in new drug applications (NDA). The rationale behind the rule change was that it could reduce duplicative trials and shorten the time required to bring new drugs to the market. However, given that the FDA is charged with ensuring that new drugs are both safe and efficacious, it still has the responsibility of validating data submitted from foreign trials. Thus, for foreign data submitted in NDAs, the FDA requires disclosure or access to the clinical investigators, research facilities, study protocol, and individual patient records.³⁹

One could argue that the FDA's effort to ensure the scientific integrity of clinical trial data bears little relationship "to the safety of the human test subjects."⁴⁰ Indeed, given the FDA's mandate to ensure the safety and efficacy of drugs, it does not appear to have an administrative rationale in protecting the rights of foreign test subjects. For instance, the safety of U.S. consumers would not be implicated if there was a lack of consent among foreign test subjects, as long as the data demonstrating safety was valid. Similarly, the efficacy of a drug would not be implicated under the scenario described above. However, by statute the FDA does indeed purport to enforce ethical standards for clinical data used to support an NDA.

There are two different pathways for studies to be accepted under FDA guidelines. In one path, a drug company can file an Investigational New Drug Application (IND), which has the effect of bringing the investigator under federal research regulations regardless of the location of the research.⁴¹ If a drug company

³⁹ See 21 C.F.R. Sec. 312.120(5)(c)(1)(2005).

⁴⁰ See Dubois at 194.

⁴¹ See Erin Talanti, *An Open Door To Ending Exploitation: Accountability for Violations of Informed Consent Under the Alien Tort Statute*, 155 U. PA. L. REV. 231, 241 (2006).

chooses not take the IND pathway and avoid direct FDA regulation, the studies used to support an NDA still must satisfy ethical standards, either the Declaration of Helsinki guidelines or regulations of the country where the research was conducted, “whichever represents the greater protection of the individual.”⁴² The FDA regulations further demand:

For each foreign clinical study submitted under this section, the sponsor shall explain how the research conformed to the ethical principles contained in the "Declaration of Helsinki" or the foreign country's standards, whichever were used. If the foreign country's standards were used, the sponsor shall explain in detail how those standards differ from the "Declaration of Helsinki" and how they offer greater protection.⁴³

Therefore, at least in theory, under this FDA regulation there should not be a “race to the bottom” problem as an underdeveloped country’s lax standards would automatically be upgraded to Declaration of Helsinki standards.

2. Umbrella of International Ethical Guidelines

The majority of European Union countries have adopted the European Convention of Human Rights and Biomedicine (CHRB) which imposes legally binding rules on the signatory countries. Article 5 of the CHRB provides the following regarding informed consent:

An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it. This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks.⁴⁴

More specifically as to scientific research, Article 16 of the CHRB provides that clinical human research can only take place if “the persons undergoing research have been

⁴² See 21 C.F.R. Sec. 312.120(5)(c)(1)(2005).

⁴³ *Id.*

⁴⁴ Council of Europe, Convention on Human Rights and Biomedicine ch. II, art. 5, 36 I.L.M. 817, 821 (1997) [hereafter CHRB].

informed of their rights and the safeguards prescribed by law for their protection . . . [and] the necessary consent as provided for under article 5 has been given expressly, specifically and is documented. Such consent may be freely withdrawn at any time.”⁴⁵ Not surprisingly, these specific provisions of the CHRB mirror the requirements of the Declaration of Helsinki.

In 1989, serious plans for the creation of a global pharmaceutical regulator began to develop at the WHO Conference of Drug Regulatory Authorities. The following year in 1990 the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was born.⁴⁶ The ICH is a collaborative effort between representatives of regulatory bodies and the drug industry to develop common protocols and regulations for ensuring the safety, efficacy, and testing of drugs. Initially, the ICH consisted primarily of representatives from the U.S., Western Europe and Japan, but now it includes observers from the WHO which provides linkage with other regions of the globe. The ICH has established ethical guidelines constituting

⁴⁵ *Id.*

⁴⁶ *History and Future of ICH: A brief History of ICH: The Need to Harmonise.* Accessed at <http://www.ich.org/cache/compo/276-254-1.html>: “Harmonisation of regulatory requirements was pioneered by the European Community, in the 1980s, as the EC (now the European Union) moved towards the development of a single market for pharmaceuticals. The success achieved in Europe demonstrated that harmonisation was feasible. At the same time there were bilateral discussions between Europe, Japan and the US on possibilities for harmonisation. It was, however, at the WHO Conference of Drug Regulatory Authorities (ICDRA), in Paris, in 1989, that specific plans for action began to materialise. Soon afterwards, the authorities approached IFPMA to discuss a joint regulatory-industry initiative on international harmonisation, and ICH was conceived. The birth of ICH took place at a meeting in April 1990, hosted by the EFPIA in Brussels. Representatives of the regulatory agencies and industry associations of Europe, Japan and the USA met, primarily, to plan an International Conference but the meeting also discussed the wider implications and terms of reference of ICH.”

“good clinical practices” in the conduct of clinical human research that meet the FDA foreign trial requirement of at least meeting Declaration of Helsinki Standards.⁴⁷

The Council for International Organizations of Medical Sciences (CIOMS) is a longstanding nongovernmental organization that was created under the auspices of WHO. A least since the 1970’s, CIOMS has specifically stated that one of its missions is to, “indicate how the ethical principles that should guide the conduct of biomedical research involving human subjects, as set forth in the Declaration of Helsinki, could be effectively applied, particularly in developing countries, given their socioeconomic circumstances, laws and regulations, and executive and administrative arrangements.”⁴⁸ Recent CIOMS ethical guidelines directed particularly at clinical trials “carried out in low resource countries” calls for the standards outlined in the Belmont Report: respect for persons, beneficence, and justice.

3. International Ethical Guidelines Without an “International” Effect

Taken as a whole, the FDA, CHRB, ICH, and CIOMS regulations all demand the application of ethical standards that are at least as robust as Declaration of Helsinki standards no matter where a clinical trial takes place. The question then becomes, do these host of ethical regulations and guidelines actually result in ethical standards being met in foreign clinical trials? The empirical evidence is discouraging. A recent study that focused on compliance with the “best proven” therapeutic efforts standard of the

⁴⁷ For instance, ICH provides the following guidelines for informed consent: “Informed consent is a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.” Id. (The Declaration of Helsinki provides similar guidelines for informed consent).

⁴⁸ See CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, “International Instruments and Guidelines” (2002), available at [http:// www.cioms.ch/guidelines](http://www.cioms.ch/guidelines)

Declaration of Helsinki in sub-Saharan African clinical trials found that only sixteen percent of studies satisfied the requirement. As a practical matter, in the event that the FDA does conduct any oversight over foreign testing sites, the oversight usually occurs after the trial is complete and thus there is no observation of methods that were used to protect research participants. In other words, the primary drug regulatory agencies (U.S., E.U., and Japan) practice of accepting foreign trials opened the door to vastly expanding the amount of globalized trials, but without a *de facto* expansion of globalized ethical protections.

III. The Body Trade—The Globalization of Human Clinical Research

A. Drugs, Drugs, Everywhere, Nor Any Drop of Profit?

Advances in biotechnology such as gene mapping and 3-D modeling of protein structures has led to a vast increase in experimental compounds that may prove to be beneficial for a variety of diseases.⁴⁹ Indeed, market valuation of pharmaceutical companies depends not only on existing sales of approved drugs, but also the “pipeline” of experimental drugs that look promising based on preliminary tissue culture and animal testing. Obviously, in order to extract value from this pipeline, companies need to perform human clinical trials to obtain market approval from drug regulatory agencies.

⁴⁹ Barry Hochfelder, *Speeding Up Drug Discovery with Imaging*, ADVANCED IMAGING PRO, September, 14, 2007. accessed at [http://www.advancedimagingpro.com/print/Advanced-Imaging-Magazine/Speeding-Up-Drug-Discovery-with-Imaging/1\\$4503](http://www.advancedimagingpro.com/print/Advanced-Imaging-Magazine/Speeding-Up-Drug-Discovery-with-Imaging/1$4503): “[R]esearchers are using 3D modeling in an effort to identify small molecules that can be used as anti-cancer agents or as antiviral inhibitors for HIV, influenza and SARS, among other diseases. The method is called computational drug design (often called structure-based or rational design). A computer is used to model how drugs interact with their targets—usually proteins. It’s done at the molecular level in 3D.” *Id.*

The initial Phase 1 studies are small and test a new drug's safety.⁵⁰ The moderately larger Phase 2 trials look for evidence of effectiveness.⁵¹ Finally, the large Phase 3 trials have to statistically prove effectiveness—it is only after this event that drug companies can expect to profit from its research efforts.

According to industry estimates, in order to bring a single drug to market, a company has to find a way to enroll 4,000 human subjects who will undergo 141 medical procedures each in 65 separate trials.⁵² Further, clinical investigators have to entice more than 100,000 people to enroll in the initial screenings for such trials as only a small percentage will show up for their appointments, and of those who do show up, only a small portion will be medically eligible. Compounding this Herculean task is the fact that American and European patients are more risk averse than previous generations and are less willing to submit to such trials.

In 1954, American parents volunteered their children as “Polio Pioneers” by the tens of thousands which meant that they were “guinea pigs” for Salk's new and unproven polio vaccine.⁵³ When the results of the massive polio trial were released in 1955 the public euphoria that ensued in the U.S. was similar to the response of winning World War II.⁵⁴ However, later, when an improperly made batch of the vaccine caused over 200 polio infections, the previously unquestioning support for this public health effort vanished.⁵⁵ Furthermore, revelations in the ensuing decades of hidden risks and unethical practices by medical researchers (e.g., see Tuskegee discussion supra) experiments

⁵⁰ Sonia Shah, *Body Hunters: How the Drug Industry Tests Its Products on the World's Poorest Patients* (2006) at 3.

⁵¹ *Id.*

⁵² *Id.*

⁵³ Laurie Garrett, *Betrayal of Trust: The Collapse of Global Public Health* (2000) at 332.

⁵⁴ *Id.*

⁵⁵ *Id.*

further solidified public aversion to clinical experiments in the U.S. Indeed, among cancer patients, who arguably have the most therapeutic incentive to volunteer for clinical trials, the participation rate is less than four percent.⁵⁶ Therefore, big pharma's collective glut of experimental drugs and challenges in securing human research subjects has literally created an intense competition for bodies on a global scale. Further, since it is difficult to bring the bodies "over here," more and more clinical trials are moving "over there" to developing countries.⁵⁷

One way to measure the globalization phenomenon is the fact that the shrinking of clinical investigators in the U.S. has been matched by an almost commensurate growth in investigators overseas.⁵⁸ Huge pharmaceutical companies like Merck, GlaxoSmithKline, and Wyeth, have estimated that in recent years they expanded their human trials outside of the U.S. and Western Europe by 67 percent.⁵⁹ However, even small startup companies without a multinational footprint can get into the globalization game by outsourcing their clinical trials to contract research organizations (CRO) that can conduct clinical trials on their behalf.

B. Severing the Umbilical Cord with Academic Institutions

As discussed above, by the late 1960s, the vast majority of U.S. experimental drugs were being tested on inmates in prison research facilities across the country. This distribution of course shifted after investigations revealed serious ethical violations in the

⁵⁶ See Shah at 4.

⁵⁷ However, for some European pharmaceutical companies, it is not cost-prohibitive to bring the test subjects to their home facilities. For instance, Swiss pharmaceutical companies have relied on the practice of recruiting subjects in the Baltic States and other European countries and flying them to test facilities located in Switzerland. Immigration, cost, and other barriers would not make this practice viable for test subjects recruited in Africa or Asia. See Sharon LaFraniere et al. *Body Hunters: The Dilemma: Submit or Suffer: 'Uninformed Consent' Is Rising Ethic of the Drug Test Boom*, WASH. POST, Dec. 20, 2000.

⁵⁸ See Shah at xi.

⁵⁹ *Id.*

prison research facilities and led to drug companies increasing their ties to academic. From an ethics standpoint, one could argue that the benefit of the enhanced pharmaceutical-university relationship is that at least it ensures that the academic institution's IRB would provide higher degree of accountability.⁶⁰ However as the size of the drug market expanded dramatically in the 1980s and 90s, drugmakers became impatient with academic centers and by the late 1990s the monetary flow from drug companies to academic centers greatly receded.⁶¹ As noted in the *New England Journal of Medicine* in 2000, "Pharmaceutical firms are frustrated with academic medical centers . . . [because of] slow review of industry proposals . . . [and] delays the starting date of trials."⁶²

Tapping on the shoulder of academic centers, and deftly not a missing step with the drug industry has been the modus operandi of a relatively new enterprise, the "contract research organization" (CRO). CROs offer to take a company's proposal for a drug trial and then rapidly deliver patients, investigators and ultimately crucial data for a NDA.⁶³ In fact, CROs have proven to be such good dance partners that this industry, which does not produce any tangible product, has grown to become a \$14 billion business with expected double-digit growth until at least the next decade.⁶⁴ Further, through years of industry consolidation, large multinational pharmaceutical corporations (there are

⁶⁰ This is not to ignore the significant body of evidence and literature citing the failures of the current IRB regime to adequately protect research subjects. But certainly this flawed regime provides significantly greater protection than to what was afforded U.S. inmates prior to the Belmont Report and to participants in many developing nations. See generally Jesse Goldner, *Dealing with Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolitionist Approach*, 28 J. L. MED. & ETHICS 379 (2000); Carl Coleman, *Duties to Subjects in Clinical Research*, 58 VAND. L. REV. 387 (2005).

⁶¹ See Shah at 4.

⁶² *Id.* at 6.

⁶³ *Id.*

⁶⁴ Dr. Jayashree, *Clinical Research Outsourcing Overview, Current Scenario, & Future Outlook*, International Biopharmaceutical Association, accessed at www.ibpassociation.org/IBPA_articles/Outsourcing.html.

currently twelve), certainly have the resources to conduct their trials in-house without the aid of academic institutions.⁶⁵

The pharmaceutical industry's desire for fast market approval, in addition to the sheer number of drug trials, is also driving the intense competition for testing bodies. For a major blockbuster drug, it has been estimated that every day a drug is delayed from entering the market there is a corresponding loss \$1.3 million in revenue. The Hatch-Waxman Act, which extends market exclusivity commensurate to the time a patented-pipeline drug is in development, does mitigate economic losses from delayed market approval, but the extension is limited to five years.⁶⁶ In addition, there are other market factors such as getting "first-mover advantage" in a particular drug segment or securing additional investment resources that drive the industry to get faster drug approval.

The drastic difference in regulatory standards and testing costs between developed and developing countries provides pharmaceutical companies immense incentive to relocate clinical trials overseas.⁶⁷ In essence, drug companies are engaging in regulatory and economic arbitrage. In coarse business terms, "the value proposition" of developing countries to drugmakers is the ability to conduct substantial amounts of research with little or no prior restraint from regulatory bodies and lower capital outlays. It goes

⁶⁵ *Id.*

⁶⁶ The Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, grants drug patent holders a period of additional marketing exclusivity to compensate for development time. The extension cannot exceed five year and is added on to the twenty years of exclusivity granted by the initial patent. *See* [Hatch-Waxman Act] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, § 156, 98 Stat. 1585 1598 (codified as amended at 15 U.S.C. 355 (2000)).

⁶⁷ Almost all large pharmaceutical companies are publicly traded and need to compete for investment to continue manufacturing and developing new drugs. To the extent a certain company's operating expenses and profit margins do not match up favorably with its competitors, it will be difficult for this company to maintain investor confidence and attract more investment dollars. Competition thus pressures the entire industry to globalize their clinical research.

without saying that the “riskiest experiments are among the first to be sent abroad.”⁶⁸

The unspoken understanding is that if the host country enforces laws the multinational company dislikes, the company could simply move its resources to a less burdensome host country.

C. Exhuming Conrad? Pfizer’s Excursion into the Heart of an Epidemic

1. Medical Crisis in Nigeria

In 1996 a massive outbreak of bacterial meningitis swept through Western Africa.⁶⁹ Particularly hard hit was Kano, Nigeria, an impoverished city of two million residents.⁷⁰ Bacterial meningitis is a serious infection of the tissue lining the spinal cord and brain.⁷¹ If not treated promptly, it has a high mortality rate. In addition to death, untreated meningitis can cause severe motor and mental damage.

At the time of the outbreak, Nigeria was run by a military dictatorship that had one of world’s worst human rights and corruption records. Therefore, despite massive oil wealth, Nigeria’s medical and social infrastructure was woefully poor.⁷² Revenues from the oil fields primarily enriched foreign oil companies and a small coterie of connected elites. Nigerian healthcare also suffered from severe “brain drain,” as a large percentage of Nigerian-trained doctors had emigrated to North America and Europe. One year prior to the outbreak, 21,000 Nigeria doctors were practicing in the US alone, approximately the same amount of doctors then in the Nigerian public service.⁷³ All of these factors

⁶⁸ See Dubois at 195.

⁶⁹ See Kristen Farrell, *Human Experimentation in Developing Countries: Improving International Practices by Identifying Vulnerable Populations and Allocating Fair Benefits*, 9 J. HEALTH CARE L. 7 POL’Y 136 (2006).

⁷⁰ See Stephens at A1.

⁷¹ *Id.*

⁷² *Id.*

⁷³ *Id.*

added up to a humanitarian crisis as the Nigerian government was ill-prepared to serve the needs of its citizens. Into this maelstrom two medical camps were set up by foreigners on the grounds of the same hospital—what happened at the camps was as different as light and darkness.

2. Kano, A Tale of Two Camps

The Infectious Diseases Hospital in Kano is a rundown compound of cinderblock buildings, some lacking electricity and running water and hence the ability to properly deal with human waste.⁷⁴ Medecins Sans Frontier (MSF) arrived first and began to treat the victims of the outbreak with the standard line therapy for bacterial meningitis, an intensive course of intravenous (IV) antibiotics.⁷⁵ MSF used an inexpensive generic antibiotic, chloramphenicol, which it had in ample supply.⁷⁶ Furthermore, chloramphenicol is recommended by the WHO as the first-line treatment for bacterial meningitis in low-income countries and which was available in ample supply.⁷⁷

Whereas MSF reacted to the outbreak as a humanitarian crisis demanding prompt medical treatment, drugmaker Pfizer saw the outbreak as an opportunity. In Pfizer's pipeline was Trovan, a broad-spectrum antibiotic projected by financial analysts to be a \$1 billion blockbuster drug if it received market approval.⁷⁸ The problem for Pfizer was that it did not have enough clinical data to get regulatory approval. The solution to Pfizer's problem was the Infectious Disease Hospital in Kano, which by February 1996 was receiving 120 new patients every day, many of them children.

⁷⁴ *Id.*

⁷⁵ *Id.* MSF is also known as Doctors Without Borders.

⁷⁶ *Id.*

⁷⁷ *Id.*

⁷⁸ *Id.*

After learning of the outbreak on the internet, Dr. Scott Hopkins, who then led Pfizer's Trovan development team, drew up a plan to test an oral form, rather than an IV version, of Trovan among the children in the Kano clinic. If the oral form of Trovan was shown to work as well as IV antibiotics in children, it would be a tremendous breakthrough in battling epidemics worldwide. Children could simply swallow a pill, rather than receiving injections which increase the risk of blood-borne diseases such as HIV and hepatitis.⁷⁹ Further, a pill would remove the need for skilled healthcare workers to assist in administration.

To take advantage of this situation, "We had to move quickly," reasoned Pfizer spokeswoman Betsy Raymond.⁸⁰ The purported reason being, "You would not be able to find those numbers of children with spinal meningitis in the U.S."⁸¹ Left unsaid by Raymond is that even if you could find scores of children in the U.S. with spinal meningitis, it would be inconceivable that anyone would approve or consent to their enrollment in an experimental antibiotics trial given the availability of proven therapies and the risks of non-efficacious treatment.

Pfizer reported that the experimental trial won rapid approval in Nigeria after an "independent review" by Nigerian authorities and approval by a Kano hospital ethics committee. Speaking of the Nigerian military government, Dr. Hopkins explained that it was, "a desperate time for them—they were happy to have anyone come in and do just about any kind of work."⁸² Thus, in the sixth week of the meningitis outbreak, a team of

⁷⁹ Many developing nations cannot afford to dispose of syringes or IV needles after each use so they are disinfected and re-used. Of course, improper disinfection will lead to the spread of blood-borne diseases.

⁸⁰ *Id.*

⁸¹ *Id.*

⁸² *Id.*

Pfizer researchers flew into Nigeria in a chartered plane and set up camp in the Kano hospital.

Tensions between MSF and Pfizer arose immediately as Pfizer's presence disrupted MSF's triage system. MSF had arranged the patients so that the sickest slept on the few available beds and benches, and the less severely sick slept on mats in outdoor tents.⁸³ For its experimental trial, Pfizer took over two of the best maintained wards, including most of the precious bed space.⁸⁴ Pfizer also drained away most of the experienced Nigerian physicians and nurses who were treating patients with MSF by paying them double what the hospital was paying. The Pfizer team spent one month in Nigeria and offered no follow-up care to the test subjects. Immediately after the trial concluded, the data was transported to the U.S and promptly submitted to the FDA.

This gambit initially appeared to work for Pfizer. Pfizer submitted the Kano data to regulators and subsequently Trovan received FDA approval. Trovan quickly became one of Pfizer's top sellers, selling over \$160 million in its first year, well on its way to its predicted \$1 billion market share.⁸⁵ But then, things started to fall apart.

3. The Unraveling of Trovan

In 1997, FDA inspectors discovered inconsistencies in data submitted by Pfizer from the Kano trial. In response to one particular FDA request, Pfizer submitted a document dated March 1996 that purported to be from the ethics committee of a Nigerian government hospital. This document stated the Nigerian ethics committee reviewed and approved Pfizer's Trovan study protocol before it was implemented in Kano. However,

⁸³ *Id.*

⁸⁴ *Id.*

⁸⁵ *Id.*

upon further inquiry, it was discovered that the document was a brazen forgery by the head Nigerian member of Pfizer's team. The referenced ethics committee did not exist in March 1996.⁸⁶ In other words, the trial never had any sort of IRB approval. These details all seemed moot, at least from the FDA's mandate, after post-marketing reports of liver failure from Trovan administration led to its severely restricted use in adults only in the U.S. and an outright ban in Europe.⁸⁷ Thus, the story of the Trovan trial in Kano was destined to die as conspiratorial ephemera, chattered about on some internet sites, but mostly ignored or dismissed as unverifiable anti-globalization hyperbole. But then an investigation by the Washington Post in 2000 shocked this story back to life.

First and foremost was the issue of informed consent, or rather the lack thereof. Many of the patients and their parents claimed that they did not know they were participating in an experimental drug trial. They simply arrived at the Kano hospital with the understanding that international medical relief workers were there to treat them.⁸⁸ This assertion was confirmed by several Nigerian healthcare workers who actually worked for Pfizer during the trial. In the words of one of these healthcare workers, "The patients did not know if it was research or not, they just knew they were sick."⁸⁹ Pfizer claimed that local nurses were trained to explain the drug trials to patients and families and that informed consent was received.⁹⁰ However, Pfizer was not able to produce any informed consent forms.

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.*

⁸⁹ *Id.*

⁹⁰ *Id.*

Further, there is evidence that Pfizer failed to switch children who were not showing any signs of improvement with Trovan, onto standard therapy.⁹¹ This breach in standard protocol allegedly led to death or severe brain damage in several children.⁹² Additionally, there is testimony that in the control group, Pfizer only gave 1/3 the recommended dose of the antibiotic ceftriaxone, essentially a non-therapeutic dose, in order to make any beneficial effects from Trovan treatment group seem greater by comparison. Compounding all of this is the assertion by the families that Pfizer never told them that they were free to refuse participation in the experimental trial and instead receive free treatment in the MSF camp.⁹³

So why does this narrative about Kano and Pfizer matter? Is not the obvious resolution to this tale that the Nigerian victims of this unethical trial will sue Pfizer for countless dollars? Will not this legal recourse act as a deterrent for such abuses regardless of whether a potential “blockbuster” drug is involved? But as will be discussed in the next section, it is not clear that the victims of Kano have any power to hold Pfizer accountable in a court of law, and certainly other multinational drug companies besides Pfizer are aware of this calculus.

IV. Using Soft Law to Play Hard Ball With The Drug Industry

A. The Challenge of Regulating Multinational Corporations

Multinational companies are notoriously difficult to regulate. In a sense they are de-nationalized as they view the world, rather than a distinct home country as their base

⁹¹ *Id.*

⁹² Given the ill-health of the children, one cannot say for certain whether they would have survived if promptly switched to standard therapy—but it is still a clear ethical violation to continue experimental treatment in the face of non-responsiveness when a proven therapy is available.

⁹³ Samantha Evans, *The Globalization of Drug Testing: Enforcing Informed Consent Through The Alien Tort Claims Act*, 19 TEMP. INT'L & COMP. L. J. 477, 480.

of operations. By using multiple facilities around the globe, corporations can strategically evade state power and certain national regulatory schemes.⁹⁴ Further, for pharmaceutical companies in particular, the relative lack of enforcement of ethical standards in developing nations means that these corporations “can operate (overseas) in a largely unregulated manner.”⁹⁵

From an international law perspective, the challenges are both “horizontal” and “vertical” in nature and the legal responses can be “hard” or “soft.” For clinical drug trials, horizontal challenges constitute problems that arise between nations trying to regulate multinational drug companies that operate across international borders. Vertical challenges are problems with unethical trials that nations, more likely developing nations with limited resources, face inside their borders.⁹⁶ “Hard-law” is represented by rule-based systems with binding authority on member states, such as the World Trade Organization (WTO). “Soft-law” represents guidelines, practices, and policies generated by non-governmental organizations for voluntary self-regulation by industry or future adoption by states.⁹⁷ These guidelines are do not have binding legal authority which is why they are considered “soft” rather than “hard.”

Addressing the ethical problems associated with globalized trials, some scholars have advocated a “hard horizontal” approach, envisioning an international organization

⁹⁴ See Dubois at 196.

⁹⁵ *Id.* See also Benjamin Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 BERKELEY J. INT’L L. 513, 532 “The legislative vacuum of medical experimentation regulations in foreign countries is intentional. While governments of these nations are desperate to bring medical research to their dying populations, their nations cannot afford such research without subsidies from multinational corporations.”⁹⁵

⁹⁶ See David Fidler, *Emerging trends in international law concerning global infectious disease control*. EMERG INFECT DIS Infect Dis [serial online] 2003 Mar. Accessed at <http://www.cdc.gov/ncidod/EID/vol9no3/02-0336.htm>.

⁹⁷ See Stathis Banakas, *A Global Concept of Justice—Dream or Nightmare? Looking at Different Concepts of Justice or Righteousness Competing in Today’s World*, 67 La. L. Rev. 1021, 1037.

with binding authority to enforce ethical standards in clinical trials on a global basis. Other commentators have argued for a “hard vertical” approach with horizontal effects, that is, an expansive reading of the Alien Tort Statute to allow U.S. courts to enforce foreign violations of ethical standards. These proposals are merit worthy in that they are advocating for more accountability and justice in globalized drug trials, but this article argues that there are practical limitations to these proposals and thus they do not offer the ethical protection for vulnerable research populations that they promise. Instead, this article proposes that horizontal soft-law techniques such as increased monitoring and reporting on globalized drug trials can be used to enforce existing hard-law drug approval regulations vertically in lucrative markets such as the U.S. and the European Union in order to deter unethical research globally.

B. Is the Alien Tort Statute a Viable Solution for Enforcing International Violations of Ethical Standards?

Countries hosting drug trials naturally have jurisdiction, or vertical control, over the companies involved in such testing.⁹⁸ However, as some commentators have pointed out, judicial protection for research subjects in developing countries is virtually absent. In response these commentators have argued for an expansive reading of the Alien Tort Statute to expand access for foreign tort claims arising from clinical drug trials to be heard in the United States:

One method of enforcing accountability in the globalization of drug testing is through litigation subjecting corporate abusers to enormous damages. Because legislative and judicial protection in underdeveloped and often corrupt host countries is nonexistent, U.S. courts should provide a forum to punish extraterritorial abuses of informed consent during

⁹⁸ See Fidler *supra* note 96.

human subject experimental research sponsored by all companies that engage in business in the United States.⁹⁹

Yet as discussed below, the proposal of opening U.S. courts to hear alien tort claims alleging abuse by multinational drug companies does not appear to be a viable solution.¹⁰⁰

But for the Washington Post investigation in 2000, Pfizer could have easily presumed that the ghost of Kano would not haunt them.¹⁰¹ As a direct result of that investigation, in 2001 the American plaintiffs' law firm Milberg Weiss filed suit in U.S. federal court against Pfizer on behalf of Nigerian children and families that participated in the Trovan trial.¹⁰² In *Abdullahi v. Pfizer*, the plaintiffs brought this action under the Alien Tort Statute to recover damages for Pfizer's alleged breach of the Nuremberg Code, the Declaration of Helsinki, the International Covenant on Civil and Political Rights (ICCPR), and the "law of nations."¹⁰³

The Alien Tort Statute (ATS) was part of the Judiciary Act of 1789 and states in relevant part: "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

⁹⁹ See Evans at 403. See also Talati at 234 ("The Alien Tort Statute (ATS) provides a viable option for these individuals, although it has not yet been successfully employed for such a purpose . . . [T]he ATS provides the most promising remedy for an individual whose right to informed consent has been violated in a clinical trial conducted in a developing country. While there are significant barriers to succeeding on any ATS claim, these barriers are not unique to the situation considered here and should not preclude a plaintiff from bringing an action under the ATS.").

¹⁰⁰ In addition to failing under a *Sosa* test, this proposal runs into other difficulties. Extraterritorial extension of U.S. regulations could run afoul of the doctrine of international comity: "International comity is a doctrine that counsels voluntary forbearance when a sovereign which has a legitimate claim to jurisdiction concludes that a second sovereign also has a legitimate claim to jurisdiction under the principles of international law." See Dubois at 196. Also, one could anticipate that the extraterritorial application of U.S. or European law onto other nations would be perceived as tantamount to legal imperialism, with the developed world imposing its rules on unwilling countries. Id at 205.

¹⁰¹ See Stephens *supra* note 1.

¹⁰² *Abdullahi v. Pfizer*, 2002 U.S. Dist. LEXIS 17436 at 4-7.

¹⁰³ Alien Tort Claims Act, 28. U.S.C. Sec. 1350.

States.”¹⁰⁴ ATS was largely forgotten and rarely used until invoked by plaintiffs in 1980 in *Filartifa v. Pena-Irala*.¹⁰⁵ Relatives of a Paraguayan who was kidnapped and tortured to death by the defendant, a Paraguayan police official, filed this suit. This opened the door to more foreigners filing ATS suits in the U.S. However, in 2004, the U.S. Supreme Court revisited ATS in *Sosa v. Alvarez-Machain* and left the door open only a crack.¹⁰⁶

In *Sosa* the Court decided that ATS was “intended only to prohibit conduct for a moderate number of international law violations that were sufficiently ‘specific, universal, and obligatory.’”¹⁰⁷ Further, the Court severely limited the application of ATS by reasoning that it only provided a means of redress if the abuse complained of had been recognized as a violation of international law when the statute was enacted: “[W]e are persuaded that federal courts should not recognize private claims under federal common law for violations of any international law norm with less definite content and acceptance among civilized nations than the historical paradigms familiar when sec. 1350 was enacted.” Additionally, the Court set forth that when applying the ATS test, a lower court must consider the practical consequences of making that cause of action available as an avenue of relief in the federal courts.¹⁰⁸

In *Abdullahi v. Pfizer*, the court recognized that “non-consensual medical experimentation does violate the law of nations and therefore the laws of the U.S.”¹⁰⁹ Citing *Sosa*, the court explained that this judicial finding provided plaintiffs with no relief as, “The law of nations generally does not create private causes of action to remedy its

¹⁰⁴ *Id.*

¹⁰⁵ *Filartifa v. Pena-Irala*. 630 F.2d 876 (2d Cir. 1980).

¹⁰⁶ *Sosa v. Alvarez-Machain* 542 U.S. 692 (2004).

¹⁰⁷ *See* Evans at 483.

¹⁰⁸ *See* Evans at 485.

¹⁰⁹ *See Abdullahi* at 9. “Thus, while informed consent has some status under international law, it is nevertheless currently unenforceable.”

violations, but leaves to each nation the task of defining the remedies that are available for international law violations.”¹¹⁰ Similarly, the court found that while the ICCPR “does bind the United States as a matter of international law, the United States ratified the Covenant on the express understanding that it was not self-executing and so did not itself create obligations enforceable in the federal courts.”¹¹¹ Because the ICCPR is not self-executing, it does not give rise to a private cause of action. In other words, even if plaintiffs proved that Pfizer violated the law of nations or the ICCPR, they would not have standing to enforce such violations under *Sosa*.

The *Abdullahi* court then turned to the plaintiffs’ claims that violations of international law as set forth in the Nuremberg Code and the Declaration of Helsinki support jurisdiction under the ATS. Addressing the Nuremberg Code, the court stated, “[T]he United States has not ratified or adopted the Nuremberg Code.”¹¹² The court concluded, “Accordingly, this Court declines to find the Nuremberg Code a binding source of international law giving rise to a private cause of action under the ATS.”¹¹³ Turning to the Declaration of Helsinki the court declared: “The Helsinki accord does not create a private right of action in U.S. federal courts and do[es] not have the force of law . . . The declaration of Helsinki . . . is a ‘mere general statement of policy that is unlikely to give rise to obligations in any strict sense.’”¹¹⁴ In dismissing the Declaration of Helsinki as binding law the court further elucidated:

[A] court is not granted a roving commission to pick and choose among declarations of public and private international organizations that have articulated a view on the matter at hand. Such declarations are almost

¹¹⁰ See *Abdullahi* at 7.

¹¹¹ *Id.*

¹¹² *Id.*

¹¹³ *Id.*

¹¹⁴ *Id.*

invariably political statements—expressing the sensibilities and the asserted aspirations and demands of some countries or organizations—rather than statements of universally-recognized legal obligations.¹¹⁵

After four years of a series of dismissals and appeals in the U.S. and Nigeria, the Trovan litigation really demonstrates the irrelevancy of international law in protecting human research subjects. The plaintiffs' claims were dismissed on grounds of both failing to state an actionable claim and *forums non conveniens*. Regarding the *forum non conveniens* claim, plaintiffs argued in vain that Nigeria was not a suitable forum as one Nigerian judge (later dismissed for accepting bribes) delayed the start of the suit against Pfizer indeterminately and the subsequent replacement judge stated that he would not hear the case for “personal reasons.” If plaintiffs failed under these set of facts in a *forum non conveniens* analysis, it is hard to imagine a scenario where they would succeed. Perhaps the situation would have to be a war-torn failed state where there was no effective government. But such a scenario it is not likely as a foreign drug company would probably not enter such a volatile environment. Therefore, it appears that multinational drug corporations are unfettered by international law or the domestic legal apparatuses in developing nations, a new strategy is needed to deter unethical abuses in human clinical trials.¹¹⁶

¹¹⁵ *Id.* at 23.

¹¹⁶ In 1999, the military dictatorship that was in power during the Trovan trial was replaced by a democratically elected civilian government. In 2000, the Washington Post expose about the drug trial caused an uproar and prompted not only lawsuits, but a Nigerian government investigation into what happened at Kano. This government report, authored in 2001, concluded that Pfizer conducted an illegal drug trial that exploited those who were not clear they were in a drug experiment and that the government never gave authorization for this trial. However, for unidentified reasons only three copies of this report were made and this report was suppressed for over five years. One of the authors of the report later stated that he received death threats in connection with producing this document. It was only through extraordinary circumstances, an anonymous leak to the international press, that this report became public five years later in 2006. Subsequent popular uproar and threats of civil unrest and rioting finally forced the Nigerian government into seeking some sort of action against Pfizer. In June 2007, Nigeria filed criminal

C. Is International Enforcement of Ethical Standards Feasible?

Several commentators have proposed that international ethical standards be established as binding hard-law and then be enforced horizontally through some kind of international institution such as the United Nations. This article clearly is sympathetic with the goals of such proposals, however it does not appear that such proposals would be viable any time in the near future. The major barriers are the matters of sovereignty and enforcement.¹¹⁷

Focusing on HIV drug trials in Africa in particular, Professor Yearby counsels that the best way to protect the interests of these populations is enforce ethical standards through an international organization.¹¹⁸ Yearby persuasively reasons that other proposed schemes to protect the interests of test populations, such as using prior agreements between African countries and foreign researchers are problematic “because there is no enforcement mechanism.”¹¹⁹ Instead, Yearby advises:

[A] possible solution . . . is the creation of an international compulsory standard of ethical protections of human subjects participating in clinical

charges against Pfizer and is seeking almost \$7 billion in a separate civil suit. This might lead one to argue that Nigeria was the proper venue for this case all along and that a legal deterrent to the actions Pfizer allegedly committed exist. However, it seems evident that but for the extraordinary leak of the 2001 report and the corresponding threat to the government’s legitimacy, Nigeria was not pursuing any claim against Pfizer. In other words, since it was not likely or predictable that Pfizer was going to be held accountable for its actions in the Trovan trial, it does not appear that a credible deterrent to future ethical abuses in similar countries exists.

¹¹⁷ See Wesley Cann, *On the Relationship Between Intellectual Property Rights and the Need of Less-Developed Countries for Access to Pharmaceuticals: Creating a Legal Duty to Supply Under a Theory of Progressive Global Constitutionalism*, 25 U. Pa. J. Int’l Econ. L. 755, 877: “The concept of enforcement, of course, is subject to interpretation. It could be argued, for example, that in the absence of the power to enforce, no legal duty can exist. On the other hand, it could also be argued that the concepts of ‘duty’ and ‘enforcement’ are in fact distinct and that duties--both in moral and legal terms--can be assumed by nations even when enforcement is impractical or abstract. In either event, this Article takes the position that treaty duties--including the duty to provide the highest attainable standard of health--are enforceable by means of a number of individual and interstate complaint systems at the domestic, regional, and international levels.”

¹¹⁸ Ruqaiyah Yearby, *Good Enough to Use for Research, but not Good Enough to Benefit from the Results of that Research: Are Clinical HIV Vaccine Trials in Africa Unjust?* 53 DePaul L. Rev. 1127, 1132 (2004).

¹¹⁹ *Id.*

trials. The standard would be drafted, implemented, and enforced by one international body. The United Nations Programme on HIV and AIDS has become the premier international organization in terms of HIV and AIDS research and would be the best place for this newly formed international regulatory body. For the organization to be effective, the standards must have penalties if they are violated, and the organization must have some ability to enforce their decisions. The organization's ability to enforce this standard will be subject to the structure of its governing document and the membership of the organization . . . With the creation of this compulsory international statement of ethics and enforcement, researchers and private funders will be held accountable for their ethical violations and deterred from committing the violation again, thus protecting vulnerable populations from exploitation.¹²⁰

A similar proposal hypothesizes that the United Nations could create something like a permanent Nuremberg tribunal to enforce international human rights.¹²¹

Focusing on transnational corporations generally and not pharmaceutical companies in particular, another article proposes that the UN establish an international organization to deal with special human rights problems posed by these companies.¹²² Certainly the benefits of having one international institution include economies of scale and predictability. A single institution could ensure that companies comply with human rights standards, whereas different nations would have redundant regulatory bodies attempting the same function.¹²³ Another proposal suggests UNESCO (UN Educational, Scientific and Cultural Organization) as being “well-positioned to create a set of international rules governing research on humans.”¹²⁴ However, this proposal recognizes that UNESCO would not be able to enforce any rules or guidelines it might formulate.

¹²⁰ *Id.* at 1151.

¹²¹ See Robert Drinan, *The Nuremberg Principles in International Law*, in George J. Annas & Michael A. Grodin, *The Nazi Doctors and the Nuremberg Code* 174, 176 (1995). The problem now is “how to get these principles, which are universally accepted, implemented and enforced throughout the world.” *Id.* at 176.

¹²² See Erin Elizabeth Macek, *Scratching the Corporate Back: Why Corporations Have No Incentive to Define Human Rights*, 11 *Minn. J. Global Trade* 101, 120 (2002).

¹²³ *Id.*

¹²⁴ See Dubois at 205.

Thus this proposal would need to rely on the enforcement mechanisms of nations in the developing world.

While all of the proposals above are merit-worthy in that they recognize the need for an international standard of ethical guidelines to address transnational actors, their shortfall is in missing a viable enforcement mechanism. The seemingly intractable problem is one of sovereignty—how can an international body enforce legal sanctions against a party if the offending party’s home country will not enforce the decision? We need only look at the difficulty facing the International Criminal Court to envision how these other proposals might not be viable.

For many years the UN General Assembly has debated and passed resolutions regarding the establishment of a permanent international criminal tribunal. Pursuant to this effort, the International Criminal Court (ICC) was established under the Statute of Rome. This Court was heralded as a “global commitment to hold . . . perpetrators of gross [human rights] violations accountable for their crimes” and indeed it has overwhelming support from most of the world’s nation states.¹²⁵ However, many have doubted whether the ICC will ever be viable as the United States has vehemently objected ICC accountability not only for U.S. government officials and military personnel, but also corporate officers engaged in business activities overseas. Commenting on the American Servicemembers’ Protection Act of 2002 (ASPA), then Under Secretary for Arms and Control and International Security, John Bolton (but more importantly he was appointed as U.S. Ambassador to the U.N. in 2005) described the Bush Administration’s expansive interpretation of the ASPA:

¹²⁵ Mark Kielsgard, *War on the International Criminal Court*, 8 N.Y. CITY L. REV. 1, 2.

This broad scope of coverage is essential to ensuring that the ICC will not become an impediment to U.S. activities around the world. We must guarantee the necessary protection to our media, delegations of public and private individuals traveling to international meetings, private individuals accompanying official personnel, contractors working alongside official personnel . . . people engaged in commerce and business abroad . . . to name just a few categories of persons.¹²⁶

As it stands, the ICC has a narrow scope of jurisdiction and will only hear four criminal charges: genocide, crimes against humanity, war crimes, and crimes of aggression.¹²⁷

However, the criminal court assumes jurisdiction only under extraordinary circumstances and is not willing to encroach upon a nation's sovereignty.¹²⁸ Further, in addition to the U.S., the two most populous and soon to be largest economies of China and India have also refused to recognize the ICC.¹²⁹

D. Using Soft Law to Exploit Hard Regulations that have International Effects

The core of this article's proposed strategy is the following: if the fruits of unethical research were denied access to the U.S. and E.U. markets, it would have the same effect as a global prohibition. In other words, this proposal argues that there is a way to get the same effect desired by the proposals discussed above, global deterrence of unethical research practices, without resorting to impractical legal schemes predicated on international enforcement bodies or quasi-universal jurisdiction in U.S. courts. In other words, rather than exclusively relying on hard law strategies, soft law measures used in

¹²⁶ *Id.* at 26.

¹²⁷ *Id.* at 7.

¹²⁸ *Id.*

¹²⁹ *U.S. Renounces World Court Treaty*, BBC NEWS, May 6, 2002, accessed at <http://news.bbc.co.uk/2/hi/americas/1970312.stm>.

conjunction with existing drug regulatory powers can be used to manipulate access to the most economically lucrative markets, the U.S., E.U., and Japan.

The logical question to be asked is, if there already exists the hard legal authority to effectuate this proposal, why do we continue to see these ethical abuses in globalized clinical trials? The problem is that structural in the sense that human research subjects, especially in developing nations, are not invested with any soft or hard power to hold drug companies accountable for their actions. As discussed above, investing these groups with hard power (e.g., ready access to U.S. courts) is problematic and not likely in the foreseeable future. However, there should be a way to invest these people with more soft power in a way that is currently not being done by international health organizations and other NGO's that are typically headquartered in London, Geneva, or Washington. With the increasing accessibility of cheap internet communication, these organizations can empower human research subjects and concerned citizens in developing nations with much of the surveillance and monitoring activities of clinical drug trials. For instance, WHO could maintain a website where alleged ethical violations can be reported with buttons translating the pages into all of the official UN languages. This reporting event could then trigger WHO officials to get a sworn statement from the reporter, which would then trigger an investigation into the alleged ethical abuses. This surveillance strategy seeks to provide a highly sensitive method of detecting ethical abuses by the minimizing both the barriers to reporting and the triggering mechanism for an investigation. Even in sub-Saharan Africa and impoverished parts of Asia, internet access is readily available through internet cafes, kiosks, and cell phones. Further,

anonymizing internet technology can be used to protect reporters of violations in authoritarian or repressive regimes.

Obviously the strategy described above would require additional resources to be spent in the area of clinical drug monitoring so the questions that arise are how will this scheme be paid for and is it really worth the expense? In terms of expense, by devolving some of the monitoring functions to those actually being tested and concerned NGO's, this would mitigate some of the expenses. Further, under the framework of the ICH which includes industry groups such as PhRMA, industry can be pressed to partially fund such an initiative because to the extent the drug industry is seen as taking the lead in self-regulating against ethical abuses in clinical trials.¹³⁰ Such an initiative can improve the image of the drug industry worldwide and can mitigate the resistance this industry faces from many social activists who characterize this industry as exploiting the powerlessness of developing nation populations for the benefit of rich countries.¹³¹ Further, drug regulatory agencies involved with ICH could increase NDA application fees to also fund such an initiative. Since the FDA has a spotty record, but actual statutory mandate, for ensuring that certain ethical standards are met in foreign drug trials, it and other drug regulatory agencies would benefit from robust monitoring and surveillance of foreign human clinical trials while they are still in progress.

The simple fact of clinical investigators knowing that they are being watched and being reported on would tend to make them more diligent in applying ethical

¹³⁰ PhRMA is the Pharmaceutical Research and Manufacturers of America and represents the pharmaceutical and biomedical industries in the U.S. It is led Billy Tauzin, former U.S. Congressman from Louisiana and is widely recognized as one of the most powerful industry lobbying groups in the U.S.

¹³¹ See generally Paul Farmer, *Pathologies of Power: Health, Human Rights, and the New War on the Poor* (2005). See also Shah *supra* note 45. This characterization has most famously been depicted in the John le Carre novel "The Constant Gardener" along with the corresponding movie with Ralph Fiennes and Rachel Weisz.

standards.¹³² Furthermore, if monitoring and subsequent investigations by the WHO or some other trusted organization does turn up evidence of ethical abuses, then this information can be made public and be used to pressure drug regulatory agencies to use the legal authority they possess to block market approval of experimental drugs that were tested unethically. Further, making such ethical allegations public after confirming their veracity would shift the burden, in the court of world opinion, onto the alleged violators to prove that their trials were conducted in an ethical manner. This *de facto* burden shifting is fair as the drug companies conducting the trials technically should already have proof of informed consent and patient protection procedures ready for viewing if they are conducting a trial consistent with international ethical norms.

E. Applying Proposal to the Trovan Case

Assuming that Pfizer's Trovan did turn out to be a \$1 billion drug that was safe and efficacious, how would this proposal affect this drug manufacturer and the status of the drug *after* it received market approval? What if Pfizer's home country, the U.S., applies the same logic it uses against the International Criminal Court and refuses to recognize international pressure that might hurt a significant economic actor? Would this scuttle the whole deterrent effect of this plan? The short answer is no. If Pfizer lost market approval to sell Trovan in other ICH members such as the E.U. and Japan, this would have a dramatic impact not only overall sales of this particular drug but also on the company's stock price.

¹³² Sociologists describe the "Hawthorne Effect" as people changing their behavior when they know they are being watched. However, the magnitude of this effect is greatest when the observation first starts and fades as the observation continues on. See Robert Fletcher et al., *Clinical Epidemiology: The Essentials*, Third Edition (1996) at 143.

A thorny social cost issue might arise if Trovan was the only drug that could treat certain diseases and if no adequate market substitute existed after it was removed from the market. This article will not go into the details of addressing this problem as this will be the focus of Part II of this paper. But very briefly, Part II proposes the stripping of intellectual property rights for the fruits of unethical drug testing under the TRIPS Agreement of the World Trade Organization. The rationale for this particular proposal is to allow generic manufacturers to step into the fray to make the beneficial drug so society can benefit without enriching a violator of ethical norms. However, generic drugs need to be evaluated for market approval as well so this could cause a gap in the beneficial drug's availability. The solution to this problem could be a Hatch-Waxman-like rule that would allow generic manufacturers to generate Abbreviated NDA data while the issue of stripping IP rights for Trovan was before the WTO hearing body. If the market determined that Pfizer had a weak case before the WTO, then generic manufacturers would take the calculated risk of developing a generic version of Trovan without knowing for certain that Pfizer might lose patent protection. If the market determined that Pfizer had a strong case, then they would likely not start developing a generic equivalent until they knew the outcome of the WTO's decision. In addition, if the U.S. still upheld Trovan's patent rights domestically, generically manufactured drugs from abroad could still depress Trovan's price through "grey market" imports.

This article acknowledges that there will likely be strong opposition in some quarters to such a proposal. One possible objection would be that this proposal is unjust because it is retroactive as it seeks to punish past behavior which in turn may unfairly take away profits from investors who think they are investing in a company with a highly

lucrative drug. However, the incentives created by this proposal are clearly *ex ante* as it provides a strong deterrence during the drug development process to not use unethical means as such actions can prove to be very costly. Moreover, there already is a baseline international ethical norm, the Declaration of Helsinki, so this offers predictability as to what standards a clinical drug trial must adhere to. Therefore, this proposal clearly enables and creates a strong market incentive for large institutional investors to conduct due diligence of drug company's ethical practices around the globe so that they can safeguard their investments. This type of market pressure alone, outside of any drug regulatory agency action, should dramatically increase ethical compliance even in developing countries.

Another possible objection is that this proposal runs afoul of the common law “takings” principle by depriving parties of valuable economic and intellectual property rights.¹³³ Under the principle of eminent domain, if the government takes property because it is useful to the public then this is a “regulatory taking” and the property holder must be compensated. However, in this proposal, these valuable rights are not being taken from the owner because they are useful to the public, they are being taken to protect human research subjects from ethical abuses. In this sense, the protection of the public from ethical abuses is a valid exercise of “police power” and thus a regulatory taking is not implicated.¹³⁴

¹³³ *What Constitutes Taking of Property Requiring Compensation Under Takings Clause of Fifth Amendment to United States Constitution—Supreme Court Cases*, 10 A.L.R. Fed. 2d 231.

¹³⁴ *Id.*

V. Conclusion

When human clinical trials are discussed in medical or pharmaceutical trade journals, numbers and statistics take on a vital role. How large was the sample size being tested on? What was the magnitude of measured effect? Was the measured effect statistically significant? How much revenue can this drug expect to generate once it receives market approval? What will be the effect on the company's stock price? Lost in all of this focus on scientific and financial numbers is the human factor. Those numbers are abstractions of events that have real impact on many individuals, families, and communities. The degree of abstraction, or separation from the human factor is even greater when those being tested on are largely invisible to the end-users of these drugs, faceless and voiceless masses in impoverished countries whose stories are not that important in richer societies. A larger sample size translates into more robust statistical evidence—it also translates into more people being exposed to risky and unproven chemical compounds. Also abstracted are the human decision-makers in drug corporations and institutional investment firms. Large revenue projections for a blockbuster drug can translate into a personal windfall for clinical investigators, corporate executives, and investors —it also represents the injustice of the benefit of high-priced drugs not flowing back to those who undergo the risk of being test subjects.

The globalization of the pharmaceutical industry and clinical drug testing is not inherently a bad thing. Indeed, without this process, cures for seemingly intractable diseases like cancer or AIDS might not be possible in the near future. However, the real and potential benefits offered by globalization in the drug industry do not mean that we

have to silently accept violations of ethical standards and the absence of accountability and justice. As Nobel-laureate economist Amartya Sen has stated:

Even though I'm pro-globalization, I have to say thank God for the anti-globalization movement. They're putting important issues on the agenda . . . My attitude to globalization is that one has to recognize first of all its inevitability, secondly its importance as an intellectual, social, political force, even as an economic force, but recognize that it can be very unjust and unfair and unequal, but these are matters under our control.¹³⁵

In other words, we are not powerless to control the actions of drug companies in testing on human subjects in developing nations. Nor should we accept the powerlessness of human research subjects to voice their concerns or hold drug companies accountable for breaches of ethical standards.

Nongovernmental organizations and international bodies such as WHO must be more creative in using their soft power to make sure that drug companies and drug regulatory agencies are following the laws that bind them within their own sovereign jurisdictions. Furthermore, these international organizations must enable low-power human test subjects in developing countries to exert some agency in the event of ethical breaches. The term globalization implies that we are all connected, and certainly in the

¹³⁵ Interview of Amartya Sen with David Barsamian accessed at <http://www.indiatogether.org/interviews/sen.htm#part2>. Sen further opined on globalization critics generally: "What we have to look at is not a kind of wholesale denunciation of globalization, which gets us nowhere. This is like King Kanute trying to discipline the sea. Quite aside from the importance of globalization, it's inescapable. It's a question of how to make it more humane and just. That requires paying attention to the underdog. I believe that virtually all the problems in the world come from inequality of one kind or another. And what we're looking at is inequality. Globalization tends to benefit most people, but not all. Some benefit greatly and others benefit relatively little. We have to see how we can make it more equitable. That requires a great deal of attention being paid to particularly labor conditions. It requires much more activism by the labor movement. It requires more reviving of cooperative attempts, and they have been successful in some countries. Bangladesh is a good example. We need more of that. It requires revision of the financial architecture of the world, because as it emerged in the 1940s it reflected a reality which is no longer true. The Bretton Woods conference in 1944 set up the IMF, the World Bank and and GATT. The WTO was the one late addition to that, but basically it's the same architecture. In the 1940s, half of the world was colonial territory. Most people were living in colonies. Democracy in the Third World was unknown. Human rights wasn't an active issue. The prospect of rapid economic growth for any poor country, especially in Asia, was unknown. The fact that people could agitate for their rights and defend the environment and demand global equity was unknown." Id.

area of clinical drug trials, citizens and corporations in developed nations directly benefit from the connection with people who serve as test subjects in developing countries. However, there needs to be more power flowing in the other direction, with test subjects being able to demand being treated with respect and credibly threatening drug companies with significant economic sanction if their rights are violated. The difficulty in legislating binding international law and overcoming issues of consensus and sovereignty should not lead us to assuming the inevitability of injustice in the drug testing arena. The legal authority exists under current drug regulatory statutes in the most lucrative economic markets to block approval of drugs that were tested unethically.¹³⁶

¹³⁶ “Unethically” at least as defined by Declaration of Helsinki standards which has become de facto the international ethical standard defining the bare minimum of ethical protections needed for human subjects in a clinical research trial.