Pharmaceutical Drug Testing in the Former Soviet Union: Contract Research Organizations as Broker-Dealers in an Emerging Testing Ground for America's Big Pharma

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PHARMACEUTICAL DRUG TESTING IN THE FORMER SOVIET UNION: CONTRACT RESEARCH ORGANIZATIONS AS BROKER-DEALERS IN AN EMERGING TESTING GROUND FOR AMERICA’S BIG PHARMA

YEVGENIA SHTILMAN*

Abstract: Developing countries are a fertile testing ground for the research and development of new drug products. Recently, Western pharmaceutical companies expanded their overseas drug testing from India and Africa to the former Soviet Union, where doctors in need of reliable income conduct clinical trials on subjects seeking access to medical care. Although U.S. government agencies monitor clinical drug trials sponsored by American pharmaceutical companies, the scope of governmental authority is effectively limited to the companies’ domestic activities. In October 2008, restrictions on the FDA’s supervisory powers were further reinforced by the agency’s substitution of the ethical research principles found in the Declaration of Helsinki with other, less subject-oriented standards. This revision threatens the health and safety of clinical trial participants in the former Soviet Union, where the medical needs of the ailing poor prevent local governments from imposing substantial restrictions on Western pharmaceuticals manufacturers. This Comment criticizes the practice of exploiting underprivileged populations for Western scientific progress, and argues that Congress must immediately respond to the FDA’s October 2008 resolution by acknowledging the Nuremberg Code as customary international law by which American pharmaceutical companies must abide.

Introduction

As the life expectancy of the average American increases, a greater percentage of the U.S. population develops debilitating conditions, in-
cluding heart disease, cancer, Alzheimer’s, and Type II diabetes. Accordingly, Americans have grown increasingly demanding of pharmaceutical companies, believing advances in medical research warrant better, less expensive drug therapies. The process of developing a new drug, however, is costly and slow—any prescription or over-the-counter drug must be approved for marketing and sale within the United States by the U.S. Food and Drug Administration (FDA)’s Center for Drug Evaluation and Research (CDER). New drugs are approved on the basis of their efficacy and safety as determined by the results of time-consuming and expensive three-phase human clinical trials. Struggling to attain sufficiently large numbers of domestic drug trial participants, American pharmaceutical companies are increasingly turning to foreign populations for test subjects and research scientists. As a result, these companies have become key players in overseas medical research.

Despite efforts to improve their image through corporate giving and public relations programs, American pharmaceutical companies are often maligned for putting profits before patients. Well-publicized


4 See About Center for Drug Evaluation and Research, supra note 3; CDER New Drug Application Process, supra note 3.


6 See, e.g., State of Readiness for 2005-2006 Flu Season: Hearing Before the Subcomm. on Oversight and Investigations of the H. Comm. on Energy and Commerce, 109th Cong. (2005) (statement of Jesse L. Goodman, Director, Center for Biologics, Evaluation and Research, Department of Health and Human Services), available at http://www.fda.gov/ola/2005/influenza0504.html (explaining that concerns about the U.S. supply of influenza vaccines incited the FDA to “stimulate interested foreign-licensed manufacturers to provide or, where needed, develop the safety and effectiveness data required for U.S. licensure”). U.S. government agencies such as the Food and Drug Administration (FDA), for example, also play a monumental role in exporting clinical drug research. See id.

7 See, e.g., Robert O’Harrow Jr., FDA Takes and End Run to Award Contract to PR Firm, WASH. POST, Oct. 2, 2008, at A1 (reporting the FDA’s attempt to hire Qorvis Communica-
allegations of failures to warn of side effects associated with medications contribute to drug manufacturers’ negative image and sometimes result in costly pre-trial settlements.\textsuperscript{8} Not surprisingly, citizens of developing nations are attractive targets for clinical drug trials, because they are generally ill-informed about judgments against American pharmaceutical companies and lack the same degree of access to their countries’ courts.\textsuperscript{9} Furthermore, despite potential safety risks, government entities in underdeveloped nations are often reluctant to regulate their citizens’ participation in experimental drug trials because these trials are often perceived as the only method of obtaining otherwise unaffordable medical treatment.\textsuperscript{10}

In recent years, countries of the former Soviet Union have attracted the attention of Western pharmaceutical companies that previously focused their clinical trials in India and Africa.\textsuperscript{11} The former So-


\textsuperscript{10} See Samantha Evans, \textit{The Globalization of Drug Testing: Enforcing Informed Consent Through the Alien Tort Claims Act}, 19 Temp. J. Int'l & Comp. L. 477, 477 (2005). The underprivileged, ailing poor tend to be unaware not only of their right to informed consent but of the very notion of such consent, which mandates that human research subjects must be “adequately informed of the risks and benefits of the trial, of their rights as participants, and their choice whether or not to participate.” See id. at 478. Wanting to provide healthcare for their citizens, governments of developing nations often turn a blind eye to the widespread abuse, injuries, and deaths that have resulted from the dangerous combination of poor people desperate for access to medicine and researchers’ desire to gather large pools of individuals to carry out clinical trials. See id.

\textsuperscript{11} See Finnuala Kelleher, \textit{The Pharmaceutical Industry’s Responsibility for Protecting Human Subjects of Clinical Trials in Developing Nations}, 38 Colum. J.L. & Soc. Probs. 67, 68–69 (2004) (explaining that countries in Africa have large pools of prospective test subjects who both qualify and are eager to participate in drug trials); Indrajit Basu, \textit{India’s Clinical
The Soviet Union offers many of the same opportunities for pharmaceutical companies that make India, a country nicknamed the “guinea pig of the world,” an attractive option. Namely, the former Soviet Union offers pharmaceutical companies three advantages. First, the area offers an abundance of clinical test subjects—volunteers who, because of poverty and poor health, are willing to gain access to healthcare by participating in risky trials without explanation of potential health consequences. Second, the former Soviet Union is home to many highly trained civilian doctors willing to carry out clinical trials on their own countrymen—even to the point of exploitation—in exchange for the steady, competitive salaries offered by American pharmaceutical companies. Third, the centralized hospital system found in many former Soviet republics facilitates the process of recruiting clinical trial participants, further lowering costs for American pharmaceutical companies conducting trials there.

Regardless of whether a clinical research study is performed in a developed or developing nation, the benefits of such research can only be achieved with negative tradeoffs, usually in the form of health risks to clinical trial participants. Compounding these patients’ vulnerability in the former Soviet Union is the lack of the strict regulations that, in Western nations, direct clinical drug researchers to comply with.

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14 See id. at 68 (discussing the advantages to foreign pharmaceutical companies of Russia’s centralized hospital system); Burden of Disease Weighs on Population, supra note 12; CROs Look to Emerging Europe to Cut Costs, supra note 12.

15 See Lustgarten, supra note 13, at 68.

ethical standards during the course of their research.\textsuperscript{17} As in other countries where underprivileged populations serve as clinical trial participants, tension has developed between the twin aims of thoroughly vetting new drugs and the importance of protecting subjects’ health and safety.\textsuperscript{18}

A principal ethical concern arising from these conflicting objectives is the question of distributive justice—the equitable distribution of the risks and benefits arising from using underprivileged test subjects in Western pharmaceutical research.\textsuperscript{19} Despite known instances of abuse of test populations in these countries, the dearth of lawsuits by test subjects against pharmaceutical manufacturers and the researchers they employ suggests that underprivileged clinical test subjects in the former Soviet Union lack access to the justice system when the research process proves harmful.\textsuperscript{20} Moreover, mere access to the courts is an insufficient guarantor of justice for international test subjects.\textsuperscript{21} Even if clinical trial subjects in the former Soviet Union were to file suit—domestically, or in the United States—against American pharmaceutical manufacturers, such plaintiffs would have very little chance of success because of the absence of positive law granting specific court jurisdiction over such cases.\textsuperscript{22}

\begin{footnotesize}
\begin{enumerate}
\item See Laughton, \textit{supra} note 5, at 191.
\item See 3 Doctors Charged in Vaccine Scandal, MOSCOW TIMES, Apr. 3, 2007, at 1. Although the former Soviet Union is notorious for keeping its own failures from the public eye, a tragic incident involving the severe illness of Russian infants was reported by \textit{The Moscow Times} in April 2007. \textit{See id.} After doctors at Independent Clinical Hospital included children with neurological disorders and chronic illnesses in a vaccine trial for British pharmaceutical company GlaxoSmithKlein, prosecutors in Volgograd began a criminal investigation of the pharmaceutical company. \textit{Id.} They discovered that GlaxoSmithKlein paid two of the three hospital directors approximately $84,000 in order to gain access to over 100 children between the ages of one and two. \textit{See id.; Andrew Osborn, GSK at Centre of Russian Vaccine Scandal}, INDEP. (London), Apr. 4, 2007, at 36. Such drug trials are illegal in Russia because the subjects were minors; furthermore, the parents of the children included in the study did not consent to their children’s participation. \textit{See Osborn, supra.}
\item See Ford & Tomossy, \textit{supra} note 19.
\item See \textit{id.} Furthermore, the Alien Tort Statute, enacted as part of the Judiciary Act of 1789, and stating in relevant part that, “district courts shall have original jurisdiction of any civil action by an alien for a tort only, committed in violation of the law of nations or a treaty of the United States,” fails to provide potential plaintiffs with a cause of action because it provides redress only where there is a violation of established international law recognized as such at the time of the statute’s enactment. \textit{See Alien Tort Claims Act, 28
Just as in India and Africa, the safety challenges presented by human experimentation in the former Soviet Union show a need for regulating human clinical trials and for balancing scientific progress with the protection of test subjects. This Comment posits that human rights violations perpetrated by American pharmaceutical companies conducting clinical drug trials in the former Soviet Union—a region largely overlooked in existing legal literature—are likely to escape judicial scrutiny. This Comment assesses the potential for existing international customary law to provide a set of comprehensive standards that would apply to these trials. Part I introduces the FDA’s drug approval process and examines the primary advantages gained by Western pharmaceutical companies who conduct clinical drug trials abroad. Part II highlights the failure of Contract Research Organizations (CROs), American pharmaceutical companies themselves, and U.S. regulatory agencies to provide for the health and safety of clinical test subjects. Part III examines the ethical debate over exporting pharmaceutical testing to the former Soviet Union as well as the role of CROs in the trial export process. Part IV presents and analyzes two sets of international guidelines that attempt to set standards for ethical experimentation on humans. The analysis in Part IV concludes that the FDA’s October 2008 rejection of certain principles espoused by the Declaration of Helsinki leaves foreign clinical trial participants more vulnerable than ever before to ethical violations. Part V argues that the Nuremberg Code, an international code of ethics, should be recognized in the United States as customary international law applicable to American pharmaceutical manufacturers in their research and development process, regardless of whether the companies conduct their clinical trials in the United States or abroad.

I. Defining the Problem

References to “Big Pharma” are well-deserved, as the American pharmaceutical industry has been the most consistently profitable sector of the economy since World War II. Before a pharmaceutical


23 See Cekola, supra note 16, at 126.

company can market a drug in the United States, the drug must obtain FDA approval. The approval process, overseen by the FDA’s Center for Drug Evaluation and Research (CDER), ensures that new drugs are safe and effective. To obtain CDER approval, a drug must undergo three phases of clinical trials as well as institutional review by the CDER. As each clinical investigation proceeds, progressively more clinical test subjects are required for each phase. A phase III clinical trial can involve up to 3000 test subjects. Large numbers of volunteers

hyperlink; then follow “IMS Health Reps. Global Biotech Sales Grew 12.5 Percent in 2007, Exceeding $75 Billion” hyperlink) [hereinafter IMS Press Release]. In 2007, the global pharmaceutical market increased 6.4%, and global prescription sales of biotech drugs, representing twenty five percent of the total pharmaceutical pipeline, increased 12.5% to more than seventy-five billion dollars. See IMS Press Release, supra.


27 See id.; ClinicalTrials.gov, Understanding Clinical Trials, http://www.clinicaltrials.gov/ct2/info/understand (last visited Apr. 24, 2009) [hereinafter Understanding Clinical Trials]. A fourth phase of clinical trials involves post-marketing studies that may reveal additional information regarding a drug’s risks, benefits and optimal use. See Understanding Clinical Trials, supra; see also Richard E. Ashcroft & A.M. Viens, Clinical Trials, in THE CAMBRIDGE TEXTBOOK OF BIOETHICS 202 (Peter A. Singer & A.M. Viens eds., 2008) (explaining that this “postmarketing surveillance phase” may also entail studies of the effect of different dosages, schedules, and length of drug administration on patients’ reactions to newly-developed drugs).

28 See Understanding Clinical Trials, supra note 27.

29 See CDER FAQ, supra note 26; Understanding Clinical Trials, supra note 27. At each phase, scientists learn the answers to different questions. See Understanding Clinical Trials, supra note 27. In Phase I trials, researchers conduct the first-ever test of the experimental drug or treatment on a small group of study participants (twenty to eighty people) to evaluate drug safety, determine a safe dosage range, and identify side effects. See id. In Phase II trials, the experimental drug or treatment is given to a larger group of study par-
are gathered to ensure that a sufficient number of participants will both meet a trial’s eligibility requirements and successfully comply with the prescribed protocol. The federal government requires that before a pharmaceutical manufacturer may begin a clinical trial on a newly-developed drug or treatment, the trial must be approved by an Institutional Review Board (IRB) to ensure it is ethical and that the risks are as low as possible and worth the potential benefits.

Pharmaceutical manufacturers have found Americans increasingly hesitant to participate in drug experiments because of skepticism about their safety. In accordance with the position taken by the American Civil Liberties Union and other organizations advocating the need for patients’ informed consent, the FDA requires that clinical test participants be willing volunteers, and federal regulation prohibits the testing of drugs in development on non-volunteer populations. These participants (100 to 300 people) to ensure efficacy and evaluate safety. See id. Phase III is used to confirm the experimental drug or treatment’s effectiveness, collect further safety-related information, and to make comparisons to other commonly used drugs or treatments. See id.

31 See Understanding Clinical Trials, supra note 27. IRBs are comprised of independent committees of physicians, statisticians, community advocates and others and are responsible for the initial approval and periodic review of research results. Id. An IRB may be “any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects.” Id. The primary purpose of such review is to assure the “protection of the rights and welfare of the human subjects.” See Cekola, supra note 16, at 132 (quoting 21 C.F.R. § 56.102(g) (2005)).
32 See Shah, supra note 30, at 4–5. Shah notes that fewer than one in twenty Americans are willing to participate in clinical trials and that less than four percent of cancer patients would participate in a new cancer drug trial. Id.
33 See 21 C.F.R. § 50.20 (2009). In an attempt to ensure the informed consent of clinical trial participants, the FDA set forth guidelines codified as General Requirements for Informed Consent in 21 C.F.R. Section 50.20. See id. The preface to these requirements states that human subjects may only participate in clinical investigations if the investigator has received their informed consent and requires that written notification provide prospective trial participants sufficient opportunity to decide whether or not to participate in the study without coercion or undue influence. See id. Although the General Requirements for Informed Consent provide that the information given to the subject shall be in language understandable to the subject or his or her representative, these regulations were enacted specifically to protect U.S. citizens from potential harms associated with experimental or untested treatment, and they make no mention of their applicability to human test subjects outside of the United States. See id.; Couture, supra note 25, at 133–34. Further suggesting that these requirements were intended only to apply within the United States is the understanding that the standard for “understandable language” is a fourth grade reading level. See Couture, supra note 25, at 138 n.62. The United States may have been targeted because of its unfortunate history of ethical violations in clinical trials. Perhaps the most notorious U.S.-based trial is the United States Public Health Service Syphilis Study, a
ernment-imposed restrictions and the difficulty drug companies have had in recruiting domestic volunteers contributed to the backup in the “pipeline” of developing drugs. An industry study in 2000 estimated that a single day’s delay in getting a major drug to market can cost a pharmaceutical company $1.3 million in unrealized sales. Pressure from shareholders to turn a profit and the large number of test subjects needed for every drug trial combine to foster intense competition between drug manufacturers for test subjects. As a result of these trends, pharmaceutical companies are bypassing academic medical centers and utilizing Contract Research Organizations (CROs)—independent contractors who are able to perform clinical trials more quickly than pharmaceutical or biotech companies.

CROs, as for-profit companies, are more aggressive and efficient in finding patients and carrying out clinical trials. CROs may even be responsible for inciting many Western pharmaceutical giants to hold

medical experiment that took place from 1932 until 1972 in Tuskegee, Alabama in which medical researchers working for the U.S. government withheld readily available medical treatment from poor black men. See Khan, supra note 22 at 883. Less well-known is the fact that clinical drug trials were performed on the U.S. prison population until ethical reforms incited Congress to outlaw the practice in the 1970s. See Shah, supra note 30, at 6; Khan, supra note 22, at 883.

See Shah, supra note 30, at 3.


See id.

See 21 C.F.R. § 312.3(b) (2008) (“Contract research organization means a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration”); Shah, supra note 30 at 6; Ken Gatter, Fixing Cracks: A Discourse Norm to Repair the Crumbling Regulatory Structure Supporting Clinical Research and Protecting Human Subjects, 73 UMKC L. Rev. 581, 618 (2005).

See Shah, supra note 30, at 6–7; Miriam Shuchman, Commercializing Clinical Trials—Risks and Benefits of the CRO Boom, 357 New Eng. J. Med. 1365, 1365 (2007); Emilie Reymond, CRO Supremacy in Clinical Research Raises Concerns, OUTSOURCING-PHARMA.COM, Oct. 3, 2007, http://www.outsourcing-pharma.com/Clinical-Development/CRO-supremacy-in-clinical-research-raises-concerns. CRO industry revenues grew from around seven billion dollars in 2001 to about $17.8 billion in 2007, and there are currently over 1000 CROs. See Reymond, supra. Among the most profitable, Quintiles, Covance, Pharmaceutical Product Development and Charles River Laboratories are billion dollar companies, with runners-up Parexel and MDS Pharma Services worth over $500 million each. See Shuchman, supra, at 1365. According to CenterWatch, a Boston-based information services company focusing on the clinical trials industry, CROs played a “substantial role” in sixty-four percent of Phase I, II and III clinical trials in 2003, as compared to only twenty-eight percent in 1993, and a study conducted by the Tufts Center for the Study of Drug Development found that ten of the largest firms had enrolled over 640,000 subjects in trials in 2004. See id.
more clinical trials overseas. This is because in addition to finding drug trial participants, CROs provide “local expertise and regulatory experience” and recruit the very doctors who perform the trials. Clinical trials that move abroad are generally held in poor countries with large ailing populations; in other words, developing countries where “ethical standards may be lax and the impoverished sick abundant.” Countries that match this description include India and others in Africa, Eastern Europe and Latin America, where the importation of clinical trials from overseas has resulted in an increase in the number of clinical investigators. From a regulatory and an ethical perspective, the danger inherent in outsourcing drug trials overseas is the threat it poses to the health and safety of human test subjects. Although clinical research trials managed by CROs for American pharmaceutical companies are subject to FDA regulation, these regulations can be circumvented more easily when trials are conducted abroad, exposing clinical trial participants to unnecessary health and safety risks as new drugs are “speeded” to the market. Furthermore, as CROs do not conduct clinical trials within “the norms and restrictions” of an academic institution’s research setting, there is an increased chance of conflict between the duty of the clinician to ensure his patients’ safety and the profitability of the CRO, the clinician himself, and the pharmaceutical company sponsoring the trial. Not surprisingly, governments wishing to attract drug companies

40 See Finlay supra note 5; Lustgarten, supra note 13, at 70–72.
42 See Shah, supra note 30, at xi; Lustgarten, supra note 13, at 69. Between 2001 and 2003, the number of U.S. clinical investigators decreased by eleven percent, simultaneously, the number of overseas clinical investigators went up eight percent. Shah, supra note 30, at xi.
43 See Gatter, supra note 37, at 618.
45 See Gatter, supra note 37 at 618–21; Gatter, supra note 44, at 351–52. Robert Gatter explains that many of the physicians conducting research for pharmaceutical companies, as well as the research institutions where the research takes place, have a financial interest in studies’ outcomes. See Gatter, supra note 44, at 351–52. The researchers and their institutions sometimes own equity in the pharmaceutical companies they work for, but more commonly, researchers and institutions enter into licensing agreements with pharmaceutical companies over scientific discoveries. See id. In either case, researchers and their institutions benefit when a drug goes to market faster; the value of equity holdings and revenues from licensing agreements goes up, and the drug companies’ success goes partially towards funding the operating costs of the researchers’ institutions. See id. Clinical trial participants therefore risk abuse at the hands of researchers who, having a financial inter-
to conduct clinical trials within their borders have strong incentives to encourage leniency in national and local oversight of the research.\(^46\) Finally, lack of uniformity in U.S. government regulation of American pharmaceutical manufacturers’ conduct across international and domestic clinical trial sites encourages these companies to export clinical trials abroad purely to escape the more stringent safety requirements imposed on experiments conducted on U.S. soil.\(^47\)

II. CURRENT REGULATIONS AND PRACTICES AFFECTING CLINICAL RESEARCH OUTSOURCING

The U.S. Department of Health and Human Services (DHHS)’s Office of Inspector General recognized the regulatory challenges posed by international clinical drug research as early as 2001, when it released a report that identified the former Soviet Union as one of several emerging markets for clinical drug trials.\(^48\) The report found that although the FDA in 2001 oversaw significantly more foreign drug research than it had a decade earlier, investigators who had not been inspected by the agency conducted a large portion of the international drug research.\(^49\) Much of this research took place in countries where neither the local IRBs nor the boards’ host countries supplied information about the review boards’ performance and where the FDA had inadequate data regarding the parties conducting clinical drug research.\(^50\) The report also found that ethics committees responsible for ensuring human subject safety in overseas trials were too disorganized to sufficiently fulfill their obligations.\(^51\) The report set forth specific recommendations for the FDA as well as for the Office for Human Re-

\(^{46}\) See Gatter, supra note 44, at 351–52.

\(^{47}\) See Molly McGregor, Note, Uninformed Consent: The United Nations’ Failure to Appropriately Police Clinical Trials in Developing Nations, 31 Suffolk Transnat’l L. Rev. 103, 120 (2007). Although McGregor specifically focuses on the lack of informed consent by trial subjects, her Note suggests, as does this Comment, that the cause of this problem “lies in the failure to achieve a uniform application of the procedure.” See id.


\(^{49}\) See id. at i.

\(^{50}\) See id. at ii.

\(^{51}\) See Gatter, supra note 44, at 353.
search Protections, with the goal of protecting the health and safety interests of human participants in non-U.S. drug trials.\textsuperscript{52}

Not surprisingly, the benefits to Western pharmaceutical coffers do not come without costs—namely health and safety risks—to their human test subjects.\textsuperscript{53} Today, the greatest obstacle to ensuring the health and safety of participants in overseas trials may be the lack of regulation over the CROs employed by Western pharmaceutical manufacturers.\textsuperscript{54} Developing, unstable countries are generally ill-equipped to oversee, much less manage, the clinical trials being held within their borders. Because there is no positive international law mandating CRO compliance with the relevant domestic laws of the clinical studies’ sponsors, the resulting “regulatory vacuum” makes it difficult for these countries to ensure the welfare of trial participants and forces them to rely on foreign data and foreign review processes.\textsuperscript{55}

American pharmaceutical companies find U.S. government support for clinical outsourcing efforts in the broad wording of relevant government regulations.\textsuperscript{56} Specifically, the U.S. regulatory scheme allows pharmaceutical companies to submit drugs for FDA approval pursuant to the Food, Drug, and Cosmetics Act even if a company’s clinical trial data are based exclusively on the results of foreign trials as long as:

\textsuperscript{52} See Rehnquist, supra note 48 at ii–iii. Other recommendations by bioethics committees have been aimed directly at companies conducting biomedical research. See Remigius N. Nwabueze, Ethical Review of Research Involving Human Subjects in Nigeria: Legal and Policy Issues, 14 IND. INT’L & COMP. L. REV. 87, 88 (2003). Two entities that have issued “copious recommendations” in response to the globalization of biomedical research are Britain’s Nuffield Council of Bioethics and the United States’ National Bioethics Advisory Committee. See id.

\textsuperscript{53} See Sarah Bahir, An International Legal System Regulating the Trade in the Pharmaceutical Sector and Services Provided by Human Subjects, 6 ASPER REV. INT’L BUS. & TRADE L. 157, 163 (2006). Regarding the trade-offs made when U.S. companies export clinical trials, Bahir explains that “[t]he benefit to pharmaceutical companies is invaluabl[e]. Not only do they get access to a ready pool of patients unavailable elsewhere, they also reduce research costs. In return for their services, research participants receive sub-standard care, unethical treatment, and unequal opportunity to benefit from prospective treatment.” See id.

\textsuperscript{54} See Rehnquist, supra note 48 at 8–15. See generally Ford & Tomossy, supra note 19 (discussing the factors a litigant may consider when bringing a lawsuit abroad rather than in the country where the clinical trial took place, but also noting the perceived corruptness of foreign tribunals). Ford and Tomossy report that in 2001, the U.S. National Bioethics Advisory Commission recommended that in the absence of an established system of clinical trials governance, trials should be approved by ethics committees in the host country and by an American Institutional Review Board. See Ford & Tomossy, supra note 19.

\textsuperscript{55} See Ford & Tomossy, supra note 19.

\textsuperscript{56} See Cekola, supra note 16, at 131.
(1) The foreign data are applicable to the U.S. population and U.S. medical practice;
(2) [T]he studies have been performed by clinical investigators of recognized competence; and
(3) [T]he data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. 57

This same regulation—21 C.F.R. § 314.106(b)—highlights the FDA’s power to self-regulate in stating that the “FDA will apply this policy in a flexible manner according to the nature of the drug and the data being considered.” 58

Perhaps the most important regulation pertaining to human trials conducted both within and outside the United States to date is the DHHS policy for the protection of human subjects, referred to as the Common Rule because it binds fifteen agencies in addition to DHHS. 59

Although the Common Rule explicitly states that research subject to regulation as defined in Section 46.102(e) that is neither conducted nor supported by a federal department or agency must nevertheless be reviewed and approved by an institutional review board (IRB), exceptions provided in the Common Rule, Sections 46.101(h) and (i), and the lack of oversight of clinical trials in developing countries limit the effectiveness of this administrative law. 60

Developing countries often lack formal

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57 See 21 C.F.R. § 314.106(b) (2009).
58 See id.
59 See Markus Schott, Medical Research on Humans: Regulation in Switzerland, the European Union and the United States, 60 Food Drug L.J. 45, 65 (2005). The policy applies to all research “involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. . . . It also includes research conducted, supported, or otherwise subject to regulation by the federal government outside the United States.” See The Common Rule, 45 C.F.R. § 46 Subpart A (2009).
60 See The Common Rule, 45 C.F.R. 46.101(a)(2). The Common Rule, § 46.102(e) states: “Research subject to regulation ... does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department’s or agency’s broader responsibility to regulate certain types of activities whether research or non-research in nature.” See 45 C.F.R. § 46.102(e). The Common Rule, § 46.101(h) states: “When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy . . . In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy.” See 45 C.F.R. § 46.101(h) (2009). The Common Rule, § 46.101(i) states:
and systematic guidelines for the safe conduct of research on humans, but Section 46.101(h) of the Common Rule might cause the FDA to overlook a pharmaceutical company’s abuse if the agency determines a developing country’s drug trial standards to be equivalent with U.S. ones and agency heads substitute foreign procedures for the U.S. requirements.\(^61\) Likewise, Section 46.101(i) of the Common Rule allows department and agency heads to waive the applicability of some or all of the safety provisions of the Code because compliance with the Common Rule is not required of U.S.-based entities such as pharmaceutical companies who conduct “purely private” research.\(^62\) The differences between the procedures used to protect drug trial subjects in the United States and those abroad suggest that under the FDA regulations, the protection of human subjects, and specifically foreign subjects, is only a “supplemental” government interest.\(^63\)

In an effort to harmonize the Code of Federal Regulations with other international standards for human clinical trials, the World Health Organization (WHO) publishes guidelines known collectively as Good Clinical Research Practice (“GCP”) to meet some of the regulatory challenges of international clinical drug testing.\(^64\) The GCP Guidelines recommend that CROs establish local review boards, obtain the

“Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy.” See id. § 46.101(i) (2009).

\(^{61}\) See Nwabueze, supra note 52, at 110–11. Until October of 2008, a U.S.-based pharmaceutical company employing a CRO to conduct research trials outside the United States needed only to comply with the stricter of the host country’s national requirements or the Declaration of Helsinki’s requirement of Institutional Review Board (IRB) monitoring and approval of trials (discussed infra). See Kelleher, supra note 11, at 84–85. However, the IRB monitoring required by the Declaration of Helsinki has been accused of being a “rubber stamp” process—were a pharmaceutical company to choose to have its CRO comply with a host country’s national requirements, the FDA would be unable to verify the compliance due to a lack of power and resources. See id. at 85.

\(^{62}\) See The Common Rule, 45 C.F.R. § 46.101(i); Schott, supra note 59, at 65.


\(^{64}\) See Gatter, supra note 44, at 357–58; Kelleher, supra note 11, at 75–76.
permission of government health ministries to pre-approve trials, counsel researchers against accepting excessive payments from drug manufacturers, and offer procedures for obtaining the informed consent of study participants. Although the WHO and other organizations advocate the tailoring of GCP provisions so that they sufficiently address specific conditions in individual countries, the merely advisory guidelines have not proven sufficient to prevent violations and abuses in clinical research taking place in developing nations. As thousands of test subjects are enrolled in clinical drug trials in the former Soviet Union, India, Africa, China, Latin America, and elsewhere, researchers and doctors are reporting failures in compliance with ethical standards. Without positive law governing clinical trials abroad, CROs have little incentive to regulate unethical or exploitative behavior by researchers. The result is an increased risk that the rapid testing and approval inherent in international pharmaceutical-product collaboration will negatively affect countries that host the overseas clinical trials of Western companies.

III. THE EMERGENCE OF THE FORMER SOVIET UNION AS WESTERN PHARMA’S NEW LABORATORY

A. The Indian Model

Much has been written in recent years about the increase in outsourcing of clinical drug trials to India and the business strategy behind

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65 See Gatter, supra note 44, at 356–57; Kelleher, supra note 11, at 75–76; Lustgarten, supra note 13, at 72.


67 See Shah, supra note 30, at 7; LaFraniere et al., supra note 17.

68 See Laughton, supra note 5, at 191.

69 See id.
the trials’ export.70 Already a favorite outsourcing destination for software development, customer service and technology call centers, India has positioned itself to become a “global hotspot” of clinical trial outsourcing while simultaneously ensuring that it captures a portion of the value it adds to foreign companies’ global research and development models.71 Regulatory maneuverings by the Indian government further enhance the country’s attractiveness as a destination for Western clinical drug trials.72

The second most populous country in the world after China, India has a large, diverse, underprivileged and drug-naïve patient population that offers easy recruitment of willing clinical trial participants who perceive the chance to participate in a drug trial as a “healthcare wind-fall.”73 The country’s inadequate healthcare infrastructure, low operating costs for Western pharmaceutical companies, and established clinical research organizations also contribute to making India an attractive destination for clinical trial outsourcing.74 Scholars are concerned about the Indian government’s ability to enforce its own regulations and oversee local ethics committees, as well as the quality of the informed consent given by researchers to trial participants.75 Simultaneously, critics fear that these tactics offer an example to countries in the former Soviet Union of how the government of an impoverished people may seek new opportunities by acquiescing to the pressures of multinational drug companies and other private organizations.76

70 See, e.g., Samiran Nundy & Chandra M. Gulhati, A New Colonialism?—Conducting Clinical Trials in India, 325 N. ENG. J. MED. 1633, 1634 (2005) (reporting that U.S. pharmaceutical companies stand to save up to sixty percent on the cost of drug trials by outsourcing them to India).
71 See Cekola, supra note 16, at 126.
72 See id. at 129–30, 145.
73 See id. at 129.
74 See id.
75 See Cekola, supra note 16, at 145; Nundy & Gulhati, supra note 70, at 1634.
76 See Nundy & Gulhati, supra note 70, at 1634–35. On the regulatory front, the Indian government amended its Patent Act in 2005, allowing foreign companies to patent pharmaceutical products there for the first time. See id. A second significant regulatory move was India’s 2005 amendment to the country’s Drugs and Cosmetics Rules to eliminate the requirement of a “phase lag” —a demand that pharmaceuticals test products in Phase III outside of India before testing them within India for Phase II trials. See id. at 1633–34. By embracing foreign pharmaceutical companies, India’s government earns compensation for its hospitals and doctors-turned-researchers. See id. at 1634; Cekoka, supra note 16, at 126.
B. Western Big Pharma’s Abuse of the Former Soviet Union: The Argument Against Outsourcing Clinical Trials

Proponents of Western drug manufacturers’ clinical trials in Russia and the former Soviet Union cite savings in the cost and time required for FDA approval as two major advantages to international trials. An emerging market for clinical trial outsourcing, Russia recently came third after China and India in a global list of the most attractive low-cost locations to run clinical trials outside the United States. Fortune Magazine reported in 2005 that American-based Pfizer Corporation conducts trials in the former Soviet Union to cut three to six months off the time it takes to get a drug to market. Overseas trials in Eastern Europe as a whole are cheaper to conduct as well—in 2005, running a drug trial in the United States cost GlaxoSmithKline about $30,000 per patient—in Romania, the cost was $3,000. The combination of speed and low cost are increasing the popularity of conducting clinical trials abroad: Jean-Paul Garnier, CEO of GlaxoSmithKline, referred to globalization as “the ultimate arbitrage” for companies like his, reporting in 2005 that a third of his company’s trials were taking place in low-cost countries and that his aim was to reach a fifty percent outsourcing rate by 2007.

Russia’s centralized hospital system contributes to the pace at which clinical trial subjects are recruited. A centralized healthcare system means that patients are conveniently hospitalized together according to symptoms and conditions, facilitating the process by which drug trial administrators identify and engage patients meeting the qualifications of their research studies. Hospitals in the former Soviet

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78 See id.

79 See Lustgarten, supra note 13, at 69.

80 See id. The former Soviet Union presents significant cost saving opportunities to foreign pharmaceutical companies largely because they are able to conduct clinical trials there earlier in the drug development cycle. See id. Striking examples of this were reported in the media as early as 2000, when the Washington Post reported that California-based Maxim Pharmaceuticals Inc. was barred from testing a new drug on Americans with liver disease until further animal testing was completed, but the company tested in Russia instead and avoided a delay that could have cost millions of dollars. See Flaherty et al., supra note 35.

81 See Lustgarten, supra note 13, at 69.

82 See id. at 87.

83 See Rehnquist, supra note 48, at 8; Lustgarten, supra note 13, at 87. The 2001 Inspector General report notes a study in Poland where “the recruitment was so fast that
Union provide CROs with eager drug trial participants and represent a boon in the large number of treatment-naïve candidates who have not built up resistance to new drugs, largely because of their infrequent use of antibiotics. Because many of the patients in these hospitals are in the advanced stages of their disease, these patients provide researchers with the ideal baseline for scientific study.

As might be expected, the chance that clinical trial participants will endure abuse at the hands of unsympathetic or overextended researchers is high, with each stage of a clinical trial presenting its own challenges. During the planning phase, CROs must ensure that the research personnel have the requisite scientific background and experience, are not overburdened by other studies, and can effectively communicate with the researchers they employ. Further risks to drug trial participants result from CROs’ failure to emphasize the importance of obtaining safe, and not simply speedy, clinical trial results. Because it is not clear whether CROs are accountable to the FDA directly or through the pharmaceutical companies sponsoring the drug trials, CROs report problems to the drug companies they work for rather than to federal regulatory agencies.

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84 See Lustgarten, supra note 13, at 70.
85 See id.
86 See Barnes, supra note 77; Reymond, supra note 38.
87 See Kristy Barnes, Managing Clinical Risk in Eastern Europe, OUTSOURCING-PHARMA.COM, Nov. 8, 2006, http://www.outsourcing-pharma.com/Clinical-Development/Managing-clinical-risk-in-Eastern-Europe. Dr. Albertas Valavicius, manager of Clinical Operations for Parexel International, a CRO based in Waltham, Massachusetts, explains that “[l]anguage issues can be problematic and paperwork needs to always be checked carefully, as well as the level of understanding of protocol etc. that staff members have.” See id. Additionally, the requisite equipment, including computers, email, fax, freezers, cupboards and touch phones, is not always available, and CROs may find themselves missing vital materials unless they have allocated additional funds for their replacement. See id. Furthermore, “[e]ven when equipment is provided by the sponsor, it often has a nasty habit of disappearing during the course of the study.” See id.
88 See Shuchman, supra note 38, at 1365. The Tufts Center for the Study of Drug Development found that CROs meet their deadlines by breaking the parts of each study (such as finding investigators and enrolling patients) into discrete steps. See id. at 1367. This process has been criticized as being a “commodification” of clinical research and has been accused of shifting researchers’ focus from the “totality of knowledge required to determine whether a drug is worth pursuing further” to data and hard deliverables. See id.
89 See id. at 1366.
In turn, the drug companies are delinquent in contacting regulatory authorities regarding health risks discovered with their products.\textsuperscript{90} For its part, the FDA’s oversight of international CRO activity is minimal at best, even for drugs manufactured by American pharmaceutical companies that need FDA approval to market and sell the drugs in the United States.\textsuperscript{91} In the former Soviet Union, CRO trial sites are springing up rapidly because the economically marginalized citizens are eager to act as trial subjects, transactional costs are low, and government oversight of CROs and the Western pharmaceutical manufacturers who employ them is limited. \textsuperscript{92}

\textbf{C. The Benefit to the Former Soviet Union of Importing Drug Trials from the United States: The (Limited) Argument Favoring Clinical Trials Outsourcing}

The potential for multi-million dollar savings by American pharmaceutical companies conducting trials in the former Soviet Union underscores the disparities between the situations of clinical trial participants in the United States and the former Soviet Union.\textsuperscript{93} However, those in favor of outsourcing drug testing argue that increased patient

\textsuperscript{90} See id.

\textsuperscript{91} See generally Rehnquist, supra note 48. The report criticized the FDA for failing to track not only the number of investigators and patients participating in international clinical trials, but also the number of international clinical sites at which American pharmaceutical companies were conducting research. See id. at 20. Although the FDA requires that international trial sites be open for spot inspection, very few inspections actually take place; in 2004, when over 500 trials were conducted at approximately 3000 Russian sites, only 100 total FDA inspections took place overseas. See Lustgarten, supra note 13, at 72. Of the Russian sites that were inspected, over thirty percent failed to follow protocol, and one in twelve international sites was identified as having failed to report adverse patient reactions. See id. This is not to say that the FDA is able to assure sufficient human-subject protection in its policing of U.S.-based trials. See id. Between 2000 and 2005, the FDA disqualified only twenty-six investigators and discounted their data only twice despite finding “serious problems” 348 times within that period. See Gardiner Harris, Report Assails F.D.A. Oversight of Clinical Trials, N.Y. Times, Sept. 28, 2007, at A1.

\textsuperscript{92} See Lustgarten, supra note 13, at 72. Because the salaries of researchers conducting clinical trials in the former Soviet Union are “lavish” by local standards—a trials investigator in Russia can make ten times his salary recruiting patients instead of working as a state hospital employee—working for Western pharmaceutical companies is an attractive option for scientists. See id. An inherent danger already documented is the bribing of doctors in state hospitals and clinics for access to patients meeting pharmaceutical company’s research study criteria. See id. Nevertheless, the December 2000 “Body Hunters” series in the Washington Post found that governments of developing countries remain eager to host pharmaceutical trials in order to infuse their health care systems with money. See Gatter, supra note 44, at 353.

\textsuperscript{93} See Lustgarten, supra note 13, at 68–70.
access to medicine and free examinations of trial participants in developing nations are satisfactory compensation for the risks assumed by trial subjects.\textsuperscript{94} Besides soliciting drug trial volunteers in the former Soviet Union, Western pharmaceutical companies also target scientists to perform the actual clinical trials.\textsuperscript{95} Proponents of the export of clinical trials view the international collaboration between Russian scientists and American pharmaceutical companies as a “win-win,” citing the combination of skilled Russian scientists eager to work for Western pharmaceutical companies and the countries’ history of scientific collaboration as rendering the former Soviet Union a natural choice for hosting the trials.\textsuperscript{96}

Organizations offering to facilitate collaboration between American pharmaceutical companies, scientists, and clinical test subjects in the former Soviet Union include the Civilian Research and Development Foundation (CRDF), a nonprofit “public-private partnership” established in 1995 and authorized by the U.S. Congress and National Science Foundation.\textsuperscript{97} The CRDF, which is based in Arlington, Virginia

\textsuperscript{94} See id. at 69–70. Western pharmaceutical companies do occasionally conduct clinical trials on underprivileged populations for drugs being developed primarily to combat those populations’ health concerns; in a project organized by the U.S. Civilian Research & Development Foundation’s GAP Services program, the Centers for Disease Control and Prevention, the World Health Organization, the U.S. Agency for International Development and their Russian partners implemented a program to combat tuberculosis, now re-emerging in Russia and other parts of the world in highly infectious, drug-resistant strains. See The U.S. Civilian Research & Development Foundation, Tackling the Threat of TB in Russia, http://www.crdf.org/stories/stories_show.htm?doc_id=298102 (last visited Apr. 9, 2009). Of course, drug trials simultaneously comprise an integral part of pharmaceutical companies’ international market development strategy; by conducting drug research in regions that are gaining purchasing power, American pharmaceutical companies begin to develop markets for the drugs should they meet FDA approval. See Rehnquist, supra note 48, at 8.

\textsuperscript{95} See Finlay, supra note 5.

\textsuperscript{96} See id. After the fall of the Iron Curtain, tens of thousands of Soviet weaponeers found themselves the unemployed targets of headhunters representing opportunities in Iran, North Korea, and terrorist organizations, all of whom offered lucrative compensation. See id. To prevent these scientists from becoming employed by countries antagonistic to the United States, the U.S. government in the 1990s began a national security campaign to “redirect” these highly trained and relatively inexpensive scientists and technicians to more peaceful pursuits, appropriating over $1 billion in research grants to former nuclear, biological and chemical and missile scientists between 1994 and 2006. See id. Today, government-sponsored “redirection” programs are losing momentum as the U.S. economy continues its economic downturn. See id. By employing large numbers of the former Soviet Union’s research scientists to conduct clinical drug trials, American pharmaceutical companies are, in a sense, taking on the responsibility that the U.S. government’s “redirection” programs once shouldered. See id.

\textsuperscript{97} See generally The Civilian Research and Development Foundation, supra note 94.
with offices in Moscow, Kiev, and the Republic of Kazakhstan, promotes international scientific and technical collaboration and the sustainability of Eurasian science and technology communities through grants, technical resources, and training. A basic tenet of the CRDF is non-proliferation, and the organization’s stated vision is “to promote peace and prosperity through international science collaboration.” An organization complementing the work of the CRDF is the United States Industry Coalition (USIC), a nonprofit made up of American businesses, associations, and research institutions that facilitates technology commercialization for the U.S. Department of Energy’s Global Initiatives for Proliferation Prevention program through redirection of weapons of mass destruction personnel towards sustainable civilian employment. USIC reports that it has facilitated business ventures worth hundreds of millions of dollars and created thousands of non-military jobs in the former Soviet Union.

IV. Customary International Law Regulating Human Clinical Testing

The lack of positive international law mandating universal protocols in human drug testing and the FDA’s ability to sanction pharmaceutical companies’ circumvention of drug trial regulations under the Common Rule does not preclude an existing international customary regime from governing clinical trials. Such a regime exists already in the Nuremberg Code, a canon intended to define “universal ethical principles that would govern all medical research in the future.” This section analyzes two alternative sources of customary international law—the Nuremberg Code (the “Code”) and the Declaration of Helsinki—and argues that the Nuremberg Code provides a sound, ethical

98 See id.; see also Finlay, supra note 5 (highlighting the work of the CRDF).
100 See Finlay, supra note 5; United States Industry Coalition: Overview, http://www.usic.net/about/index.cfm?cid=1 (last visited Apr. 9, 2009).
101 See generally United States Industry Coalition: Overview, supra note 100.
103 See Schott, supra note 59, at 47. Schott refers to the Nuremberg Code as “the first international legal document” among authorities setting forth ethical standards for international clinical testing. See id.
procedure that should be followed by Western pharmaceutical companies engaged in exporting clinical drug trials to less-developed countries.

The Nuremberg Code consists of ten directives for human medical experimentation.104 American judges set forth the Code in 1947, to-


The Nuremberg Code states:

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, overreaching, 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 reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

   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.

2. 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.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. 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.
together with the verdicts of the Nuremberg “Doctors’ Trial”—the first of twelve trials against Nazi officials in which medical doctors, who carried out horrific, unethical medical experiments on humans, were found guilty of committing war crimes and crimes against humanity.\textsuperscript{105}

Today, the Nuremberg Code is widely regarded as the preeminent source of law and ethics on human testing.\textsuperscript{106} It has been labeled the “most accepted” and the “most cited” code of medical ethics.\textsuperscript{107} Unlike the FDA regulations and the Declaration of Helsinki, the Nuremberg Code places the responsibility of ensuring ethical medical experimentation directly in the hands of researchers.\textsuperscript{108} This is because the provisions of the Nuremberg Code are directed at scientists and researchers rather than at the institutions they represent.\textsuperscript{109} Furthermore, the Code does not require that research be monitored and approved by independent parties.\textsuperscript{110}

Opening with the declaration that “[t]he voluntary consent of the human subject is absolutely essential,” the Nuremberg Code prioritizes the welfare of test subjects and emphasizes the need for their informed consent. 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.


\textit{See Bartha Maria Knoppers & Madelaine Saginur, \textit{Bio-banking}, in \textit{The Cambridge Textbook of Bioethics} 167 (Peter A. Singer & A.M. Viens eds., 2008); Sharon Perley et al., \textit{The Nuremberg Code: An International Overview, in The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation} 149, 149 (George J. Annas & Michael A. Grodin eds., 1992); Laughton, \textit{supra} note 5 at 184–85.}\textsuperscript{106}

\textit{See Laughton, \textit{supra} note 5, at 184 (citing Joel Levi, \textit{Medicine, The Holocaust, and The Doctors’ Trial}, in \textit{Bioethical and Ethical Issues Surrounding the Trials and the Code of Nuremberg: Nuremberg Revisited} 111, 116 (Jacques J. Rozenberg ed., 2003)). Like the Nuremberg Code and other international codes and agreements, the Hippocratic Oath assigns the task of making decisions regarding human experiments to the clinician. \textit{See id.} at 182. In taking the Hippocratic Oath, physicians pledge to provide care for the benefit of their patients; however, the exact benefit to be derived by the patient is to be determined by the physician. \textit{See id.}\textsuperscript{107}

\textit{See Cekola, \textit{supra} note 16, at 144.}\textsuperscript{108} \textit{See id.}\textsuperscript{109}

\textit{See id.} Specifically, the Nuremberg Code states in the second paragraph of Provision 1 that “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.” Nuremberg Code, \textit{supra} note 104, ¶ 1.
To further protect their safety and welfare, the Code forbids the waiver of its principles by trial participants and requires: 1) proper preparations and facilities to be in place such that the subject is protected from “against even [a] remote possibility of injury, disability, or death”; 2) a valid research design to procure beneficial results that cannot be obtained by any other methods or means of study; 3) that the experimental design be “based on the results of animal experimentation and a knowledge of the natural history of the disease or clear problem under study”; 4) the avoidance of “all unnecessary physical and mental suffering and injury” and the absence of any “a priori reason to believe that death or disabling injury” would result from experimentation; 5) benefits that outweigh trial-related risks; 6) the presence of a qualified researcher who is prepared to terminate an experiment if it “is likely to result in the injury, disability, or death of the experimental subject”; and 7) the subject’s ability to end the experiment should he reach a physical or mental state where he is unable or unwilling to continue.

In spite, or perhaps because of its humanitarian aims, the Nuremberg Code has not been universally embraced by the international community. The United States has neither ratified nor adopted the Nuremberg Code. Instead, U.S. federal regulations depart from the Code’s emphasis on the researcher’s authority in that they place responsibility with research institutions and IRBs rather than with the researchers themselves. As a result, whether clinical trial participants

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111 See Nuremberg Code, princi. 1, supra note 104. Merely obtaining the informed and voluntary consent of a test subject is insufficient under the Code, however, because the Code requires that all of its principles relating to the welfare of subjects be satisfied even before the subjects’ consent is sought. See George J. Annas, The Changing Landscape of Human Experimentation Nuremberg, Helsinki and Beyond, 2 HEALTH MATRIX 119, 121 (1992).

112 See Nuremberg Code, supra note 104, ¶¶ 2–10. The provisions in paragraphs 5 and 9 are of special importance because no subsequent assertion of ethical standards to be observed in human clinical trials contains them. See Annas, supra note 111, at 121; Schott, supra note 59, at 47.


115 See Laughton, supra note 5, at 194.
will suffer violations of the rights enumerated in the Code depends on the ethics of the researcher performing the trial—a researcher whose priority may often be to achieve specific scientific results.\textsuperscript{116}

The Code lacks the force of positive law and has never served as the sole basis for damages awards or the discipline of a scientist or researcher.\textsuperscript{117} However, it is recognized as “an authoritative statement of the fundamental rights of research subjects in all nations,” and is produced as part of international criminal trials.\textsuperscript{118} In fact, courts in the United States have allowed the Code to be introduced as evidence of ethical principles existing in customary international law.\textsuperscript{119}

A combination of the Nuremberg Code’s lack of legal force and medical researchers’ concern that the Code is too “legalistic” and therefore insufficiently supportive of scientific progress led researchers to create a separate set of ethical standards after the Second World War.\textsuperscript{120} In July of 1964, the World Medical Association (WMA) incorporated as a non-profit educational and scientific organization in the State of New York, thus establishing the legal and financial status of the WMA in the United States.\textsuperscript{121} That same year, the WMA adopted the

\textsuperscript{116} See id. at 193 (citing Nuremberg Code, supra note 104, ¶ 1, 10 (“assigning to the researcher both the responsibility of obtaining informed consent and of determining when the experiment should be terminated”)).


\textsuperscript{118} See Annas, supra note 117 at 201; Nicholas A. Christakis & Robert J. Levine, Multinational Research, in 3 ENCYC. OF BIOETHICS 1780 (Warren Thomas Reich ed., 1995).

\textsuperscript{119} See Abdullahi v. Pfizer, Inc., No. 01 Civ. 8118, 2002 WL 31082956 at *3 (S.D.N.Y. Sept. 17, 2002); Grimes v. Kennedy Krieger Inst., 782 A.2d 835, 849 (Md. 2001). In its discussion of the Nuremberg Code, the Grimes court stated that “the Nuremberg Code, at least in significant part, was the result of legal thought and legal principles, as opposed to medical or scientific principles, and thus should be the preferred standard for assessing the legality of scientific research on human subjects. Under it, duties to research subjects arise.” See Grimes, 782 A.2d at 835. The court also stated that the Code was meant to be applied internationally and never expressly rejected in the United States. See id. at 849. In Abdullahi, the court allowed the introduction of both the Declaration of Helsinki and the Nuremberg Code as evidence of principles of customary international law, but concluded that neither was “sufficiently universal” to establish a claim. See Abdullahi, 2002 WL 31082956, at *5; Laughton, supra note 5, at 197.

\textsuperscript{120} See Laughton, supra note 5, at 194–97.

\textsuperscript{121} See The World Medical Association, About the WMA, http://www.wma.net/e/about/index.htm (last visited Apr. 9, 2009). The WMA’s stated purpose is to “serve humanity by endeavoring to achieve the highest international standards in Medical Education, Medical Science, Medical Art and Medical Ethics, and Health Care for all people in the world.” Id.
Declaration of Helsinki, its best-known policy statement. The Declaration of Helsinki is less trial participant-focused than the Nuremberg Code and is regarded by some as the definitive statement of medical ethics regarding medical research, in part because it was signed by the United States and incorporated into the FDA’s regulations for overseas clinical research in 1975.

The FDA’s position vis-à-vis the Declaration has changed, however, and the agency replaced the Declaration’s principles with a requirement of Good Clinical Practice in its regulation of the acceptance of non-IND (Investigational New Drug) foreign clinical studies. Some have argued that this move indicates that the FDA views ethical considerations as “expendable” when trial subjects live in the developing world, warning that the FDA’s rejection of the Declaration’s principles increases the potential of ethical violations in international trials. Although the FDA’s rejection of the Declaration’s principles deals a significant blow to the framework ensuring American pharmaceutical companies’ ethical conduct overseas, it must be noted that the Declaration, unlike the

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123 See Declaration of Helsinki, supra note 122; Shah, supra note 30, at 76; Nuffield Discussion Paper, supra note 122, at 65; Laughton, supra note 5, at 194.

124 See Human Subject Protection; Foreign Clinical Studies Not Conducted Under an Investigational New Drug Application, 73 Fed. Reg. 82, 22800 (Apr. 28, 2008) (to be codified at 21 C.F.R. pt. 312). In collaboration with WHO, the Council for International Organizations of Medical Sciences (CIOMS) published its own ethical guidelines in 2002. See COUNCIL FOR INT’L ORG. OF MEDICAL SCI., INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (2002), http://www.cioms.ch/frame_guidelines_nov_2002.htm. The CIOMS Guidelines were intended to address the special circumstances that arise when applying the Declaration of Helsinki to research undertaken in developing countries and were revised in 1991, 1993 and in 2002. See Nuffield Discussion Paper, supra note 122, at 4. The CIOMS Guidelines approvingly reference the Declaration, in essence capturing the notion that “on the whole [the 1964 Declaration of Helsinki] corrects what in the Nuremberg Rules was circumstantial, related to Nazi crimes, and places these Rules more correctly in the context of generally accepted medical traditions.” See Annas, supra note 111, at 123 (citing W. Refshauge, The Place for International Standards in Conducting Research for Humans, 55 BULL. WORLD HEALTH ORG. 133, 137 (1977)). However, as of October 2008, the FDA removed references to the Declaration of Helsinki from § 312.120. See 73 Fed. Reg. 82, 22800–01.

Code, always prioritized the protection of the scientific process over the health and safety of clinical trial participants.\textsuperscript{126} Whereas the Code holds a trial subject’s voluntary consent “absolutely essential,” the Declaration asks that a trial participant give his voluntary consent “if at all possible.”\textsuperscript{127} Furthermore, the Declaration’s encouragement of peer review of research protocols implies that a subject need not give informed consent to participate in medical research if the physician submits his reasons for not obtaining consent to an independent review committee.\textsuperscript{128} Finally, the Declaration only feebly protects subjects’ interests in stating that independent review committees “must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards.”\textsuperscript{129}

Critics of the Declaration accuse it of “marginalizing” the Code, and view its true goal as replacing the Code’s human rights-based agenda with a comparatively “lenient medical ethics model that permits paternalism.”\textsuperscript{130} Some of the Declaration’s most vehement opponents have an even more radical outlook; they view the Declaration as a continuation of the legacy of Nazism with the Code itself as the victim.\textsuperscript{131} Though some hold the Declaration to be the more authoritative source of customary international law, the combination of its recent rejection by the FDA and its failure to advocate to the fullest for the protection of trial participants renders it the inferior source of protection clinical trial participants.\textsuperscript{132} Therefore it is the Nuremberg Code that should be accepted by the United States as the customary international standard to be implemented in regulating U.S. pharmaceutical companies’ export of clinical drug trials.\textsuperscript{133}

\textsuperscript{126} See Khan, supra note 22, at 887–89; Laughton, supra note 5, at 195–96.

\textsuperscript{127} See Laughton, supra note 5, at 195. Furthermore, the Declaration delineates circumstances under which researchers may conduct clinical trials without obtaining patients’ informed consent. See Annas, supra note 111, at 123. For instance, the Declaration (unlike the Code) allows a trial subject’s proxy to give consent on behalf of the patient where the patient is legally or physically incapacitated. See Laughton, supra note 5, at 195.

\textsuperscript{128} See Annas, supra note 111, at 123. Some detractors of the Declaration believe that “[t]he Declaration of Helsinki . . . undermined the primacy of subject consent in the Nuremberg Code and replaced it with the paternalistic values of the traditional doctor-patient relationship.” See Seidelman, supra note 105, at 1465.

\textsuperscript{129} See The World Medical Association, Declaration of Helsinki (2008), supra note 122, ¶ 15.

\textsuperscript{130} See Annas, supra note 111, at 122.

\textsuperscript{131} See Seidelman, supra note 105, at 1465.

\textsuperscript{132} See id. at 1465–66; Wollensack, supra note 102, at 769–71.

\textsuperscript{133} See Wollensack, supra note 102, at 769–71.
V. The Solution: The United States Must Recognize the Nuremberg Code as International Customary Law Regulating Human Clinical Testing

Clinical trial participants in developing countries who fall victim to unethical treatment in international scientific investigations must have recourse under customary international law.134 Ideally, such victims would be able to establish a cause of action by demonstrating the violation of one or several of the principles of the Nuremberg Code, a cause of action that would allow the victim to hold accountable the researcher conducting the drug trial as well as the pharmaceutical company sponsoring the trial and the CRO overseeing the researcher’s activities.135 To better understand why this solution is the most viable, competing ideas must be examined.136

One way to ensure the health and safety of clinical research subjects is to centralize the review of clinical trials.137 Supporters of this solution claim it will enable the concentration of scientific expertise as well as improve the efficiency of the review process.138 However, it is uncertain whether a centralized process would be more efficient, especially because it is unclear who would manage the centralizing—a federal agency, a private entity subject to federal oversight, or something in between.139 Criticisms of this solution focus on the difficulty of incorporating regional and institutional variations into the regulation process, as well as the risk that a centralized authority may increase the chance of self-interested behavior on the part of researchers, leading to an even more adversarial relationship between clinical researchers and regulations.140

Because of these concerns, Professor Ken Gatter suggests that “fine-tuning and better enforcement of existing regulations will not remedy the underlying structural instability resulting from the conflicting norms.”141 Rather than instituting a new system of government oversight, opponents of a centralized system, such as Professor Robert Gat-

134 See id.
135 See Gatter, supra note 44, at 351–52; Wollensack, supra note 102, at 769–71.
136 See Wollensack, supra note 102, at 769–71.
137 See id.
138 See Gatter, supra note 37, at 620.
139 See id.
140 See id.
141 See id. at 623. The specific conflicting norms Professor Ken Gatter refers to are “informed consent with its normative basis in autonomy, the research community with its utilitarian normative structure; and the fiduciary model of the therapeutic clinical setting.” See id.
ter, suggest that conflicts of interest in human research may be avoided by researchers’ self-regulation and only minimal prohibitions; the concern is that an extensive system of prohibiting financial conflicts would only lead to strategic behavior to evade them. Another proposed solution is for Congress to establish a voluntary plaintiff’s forum in the United States under the Alien Tort Statute (ATS). Proponents of this approach suggest that Congress could choose to recognize either of two international doctrines, the International Covenant on Civil and Political Rights or the Nuremberg Code, to create a right of action under the ATS.

A solution that subscribes to Robert Gatter’s theory and harnesses the benefits of the ATS while avoiding the criticisms directed at the concept of a centralized review system is for the United States to recognize the Nuremberg Code as customary international law, permitting plaintiffs a cause of action against American pharmaceutical companies when their rights under the Code are violated. However, unlike Wollensack’s proposal to create the forum within the United States, the ideal solution would not require the specific designation of a particular venue for the forum. A U.S.-based forum would place unnecessary hardship on injured clinical drug trial participants who would, for the most part, be unable to travel to the United States to appear in court. Instead, an acceptable forum should be deemed to be any country where a pharmaceutical company conducts its clinical research—aft...

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142 See id. at 623, 626. Professor Robert Gatter also warns that as long as some countries willingly ignore ethical guidelines to obtain the short-term financial benefits that come with hosting human trials, even a coalition of countries cooperating to strengthen domestic drug laws will be unlikely to protect human drug trial participants. See Gatter, supra note 44, at 363–64.
143 See Alien Tort Claims Act, 28 U.S.C. § 1350 (2000); Wollensack, supra note 102, at 769.
145 See Wollensack, supra note 102, at 769.
146 See id. at 769–71.
147 But see id.
148 See id.
Conclusion

Despite the Nuremberg Code’s shortcomings, the standards it sets forth provide a viable solution to prevent the unethical treatment of clinical trial participants by CROs employed by American pharmaceutical companies.\textsuperscript{149} This is because the existing customary international law presented by the Code places the onus of ensuring ethical treatment of trial participants on the very clinicians performing the trials.\textsuperscript{150} The Code’s principles are clear, succinct, and humanitarian in nature, and the Code is already perceived as constituting an international customary regime.\textsuperscript{151} This solution is not inappropriately bold, as the Nuremberg Code’s principles already “set the framework for United States federal regulations as well as . . . international guidelines.”\textsuperscript{152} The citizens of the former Soviet Union, like all participants in drug trials, deserve not only a means of asserting their right to ethical treatment, but also a clear statement of what that ethical treatment should be.\textsuperscript{153} By acknowledging the Nuremberg Code as customary international law and not merely a set of guidelines, the United States government would shift the burden of regulating drug trials to researchers, and would simultaneously make American pharmaceutical companies and the CROs they employ accountable for the research protocols they write.\textsuperscript{154} Adoption of the Code as customary international law would provide a right of recourse to clinical trial participants in the former Soviet Union and around the world, thus ensuring the drug test subjects of American Big Pharma the protections of the Nuremberg Code.\textsuperscript{155}

\textsuperscript{149} See id.

\textsuperscript{150} See Cekola, \textit{supra} note 16, at 144.


\textsuperscript{153} See Gatter, \textit{supra} note 37, at 623–27.

\textsuperscript{154} See Gatter, \textit{supra} note 44, 351–52; Wollensack, \textit{supra} note 102, at 769–71.

\textsuperscript{155} See Wollensack, \textit{supra} note 102, at 769.