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CLINICAL TRIALS: EMERGING ISSUES REGARDING GLOBALIZATION OF
PHARMACEUTICAL RESEARCH; INSURANCE; INFORMED CONSENT;
SECURITIES LITIGATION; AND PUBLIC POLICY

By

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INTRODUCTION

In the last few years, there have been important developments that bear on the law governing clinical trials and attendant liability, insurance, regulatory, and policy issues. The developments include the globalization of pharmaceutical research, increased news coverage, the emergence of various public policy questions, and a reported increase in litigation of clinical trial issues, *see, e.g.*, Nora Lockwood Tooher, *Clinical Trials Lawsuits on the Rise Across the Country*, St. Louis Daily Record & St. Louis Countian, Aug. 31, 2005, available at http://findarticles.com/p/articles/mi_qn4185/is_20050831/ai_n14913350/print. Key developments discussed in this article include¹:

I. The Globalization of Pharmaceutical Research

- A. Informed consent issues
- B. Insurance coverage issues, including the question of "admitted" insurers
- C. The EU Clinical Trial Directive
- D. Good Clinical Practice
- E. The French Law on Protection of Persons Undergoing Biomedical Research
- F. The Issue of Extraterritorial Application of U.S. Laws and Regulations
- G. Alien Torts Claims Act Issues, Including the Pfizer case and its Nigerian Clinical Trial

II. Tort Liability Issues

- A. Products Liability, including Failure to Warn
- B. Informed Consent, and Related Medical Malpractice Issues

¹ Liability and insurance issues attendant to clinical trials are also discussed in Michael Traynor, *Clinical Trials: Emerging Products Liability and Insurance Issues*, in ALI-ABA Course of Study Materials: Products Liability, July 19-20, 1996, at 179, available at WL SB16 ALI-ABA 179. *See also* Michael Traynor, *As Manufacturers Seek Approval for More New Pharmaceuticals, Issues Such as the 'Learned Intermediary' Rule Will Emerge in Litigation Involving Clinical Trials*, Nat'l L.J., Nov. 18, 1996, at B6. Although these articles remain generally relevant, commentary about and developments in clinical trials have significantly increased since they were published. In addition, basic information about the issues and liability and risk issues is more readily available. *See, e.g.*, NIH, <http://www.clinicaltrials.gov/ct/info/resources;jsessionid=926E02C5D0CAFA1B356A8F524BD26EA6>; Areta L. Kupchyk & Josephine M. Torrente, *Legal Issues During Research and Development*, *Pharmaceutical Law 2006: Across the Product Life Cycle*, 878 PLI/Pat 9 (2006); Clinton D. Hermes & Joanna L. Bergmann, *Counseling on the Ethical and Legal Issues in Biomedical Research*, *Pharmaceutical Law 2006: Across the Product Life Cycle*, 878 PLI/Pat 49 (2006); David M. Fox, *Basics of FDA Approval*, *Pharmaceutical Law 2006: Across the Product Life Cycle*, 878 PLI/Pat 267 (2006); Michael J. Malinowski, *Ethics in a Global Biopharmaceutical Environment*, 5 Santa Clara J. Int'l L. 57 (2006); Finuala Kelleher, *The Pharmaceutical Industry's Responsibility in Protecting Human Subjects of Clinical Trials in Foreign Countries*, 38 Colum. J.L. & Soc. Probs. 67 (2004); Sullivan Group, *2004 Human Clinical Trials Liability Primer*, available at http://www.sullivangroup.com/news/publications/2004_Human_Clinical_Trials_Liability_Primer.pdf.

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I. The Globalization of Pharmaceutical Research

Conducting clinical trials abroad is a recent phenomenon that has rapidly gained momentum. William DuBois, *New Drug Research, the Extraterritorial Application of FDA Regulations, and the Need for International Cooperation*, 36 Vand. J. Transnat'l L. 161, 167 (2003). The number of clinical trials conducted outside the United States increased exponentially in the 1990s, from 271 in 1990 to over 4,400 in 1999. *Id.* This increase is partly due to relaxed U.S. rules governing drug research, which now allows foreign data to be used. *Id.* See also Kupchyk & Torrente, *supra*, at 23. The proliferation of U.S. biotechnology companies conducting international clinical trials has created a unique set of liability, insurance, and ethical issues, which are outlined below. See, e.g., Samantha Evans, *The Globalization of Drug Testing: Enforcing Informed Consent Through the Alien Tort Claims Act*, 19 Temp. Int'l & Comp. L.J. 477 (2005); Frank F. Goudsmit, *Navigating the International Insurance Market*, J. Biolaw & Bus., Vol. 6, No. 3, 2003.

A. Informed consent issues

Given the increasing number of clinical drug trials conducted in developing countries, Evans, *supra*, at 477, obtaining informed consent in these nations has become increasingly challenging as well as problematic, especially, as is often the case, when research subjects are uneducated, extremely poor, do not speak English, and have very different cultures. See, e.g., Jonathan Todres, *Can Research Subjects of Clinical Trials in Developing Countries Sue Physician-Investigators for Human Rights Violations?* 16 N.Y.L. Sch. J. Hum. Rts. 737, 757 (2000). To further complicate matters, researchers often treat clinical subjects as patients, so the subject volunteers may assume that the researcher will decide what is in their best interest. See Benjamin Mason Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 Berkeley J. Int'l L. 513, 518-19 (2002). Women and children are especially vulnerable to coercion because of their comparative status and societal powerlessness. *Id.* at 540.

Critical components of informed consent may be lost easily in translation between languages. In one instance, consent forms used in AZT clinical trials in Thai and English differed greatly in the descriptions of study design. Todres, *supra*, at 761. The English version explained that one-half of the study group would receive a placebo, while the Thai version stated that one-half of the study group would receive a "comparison drug." *Id.* Because clinical trials may be the only vehicle for receiving treatment for life-threatening diseases such as AIDS in

developing countries, it is imperative that volunteers receive adequate and truthful information.

Currently, many developing countries lack any ethical review standard or mechanism to protect research subjects involved in clinical trials. See DuBois, *supra*, at 195. There have been calls for developed countries to help developing ones create a set of enforceable rules to protect human research subjects on such vital matters as informed consent. *Id.* at 205. One scholar has proposed that an international body, such as UNESCO, issue a set of international rules governing human research testing. *Id.* Others have recommended the United Nations as a model organization for developing such rules because of its support structures and ethical credibility. See Meier, *supra*, at 552. Additional credible alternatives include creating international panels or institutions. It is important that international health professionals gain a reputation for credibility and ethical practices rather than one for deception if biotechnology companies employing these professionals wish to continue to conduct credible clinical trials abroad.

B. Insurance coverage issues, including the question of "admitted" insurers

Insurance is an important consideration for biotechnology companies conducting research anywhere because it gives necessary protection in the event that a research subject is injured during the course of the clinical trial. Goudsmit, *supra*. However, international clinical trials require special consideration because each country may have different requirements regarding liability insurance. See Sullivan Group, *supra*. A biotechnology company conducting research in foreign countries should also consider obtaining products liability insurance in the event that the use of a product causes bodily injury. See Goudsmit, *supra*; David T. Case, Julia Reynolds Johnson, & Anand D. Nair, *Life Sciences Companies and Liability Insurance for Clinical Trials Conducted Abroad*, Biotech Briefing (July 2006) (Newsletter of the Biotechnology Committee, ABA Section of Science & Technology Law) (includes discussion of TeGenero clinical trial in London and related insurance issues), *available at* <http://www.klgates.com/files/Publication/69c5eeb9-80a3-43a1-ba34-3ff4b9f430d7/Presentation/PublicationAttachment/7a47960c-1682-4f1b-9feb-43ddc8f05a76/Biotech.pdf>. Clinical trials liability insurance should be available to cover a life science company during the policy term, and if so, should be extendable to cover clinical investigators and other employees. Sullivan Group, *supra*.

Researchers must look at insurance requirements specific to each country in order to ensure that clinical trials comply with foreign requirements. See *Clinical Trial Liability*, Commerce Banc Insurance Services, available at http://insure.commerceonline.com/commercial/1st_clinicalTrial.cfm. Recently, attempts have been made to unify the approach of protecting patients outside the United States, which creates new issues for obtaining the appropriate insurance policies. *Id.*

Local laws in each country govern which insurance carriers are authorized to conduct business there. These insurance carriers are correspondingly termed "admitted" or "not admitted." *Id.* "Admitted" coverage refers to an insurance carrier authorized to conduct business under local insurance laws, whose policy is written and issued in the specific locale. *Id.* Coverage on a "non-admitted" basis may be more flexible, but the majority of countries where clinical trials are conducted require "admitted" coverage. *Id.*

Although test sites usually will inform sponsor companies of their insurance and indemnification requirements, if they do not do so, the sponsoring company should ask them. Given the small number of insurers that can handle international placements for biotechnology companies, international insurance options can be limited. Major challenges to securing insurance for foreign clinical trials not only availability and coverage but also time and cost. Commerce Banc Insurance Services, *supra*.

Biotechnology companies considering insurance providers should look at the following issues appearing on policy forms: claims made versus occurrence forms, retroactive dates, limits, exclusions, retentions or deductibles, coverage extensions, and coverage territory. Companies should also view factors such as outside parties, the risk of a particular trial, risk assumed via contract, limits chosen by a peer group, the experience and expertise of the broker whom they are using, and industry experience of insurers when determining the appropriate insurance coverage, limits, and deductibles *Id.*

In addition, insurance underwriters should scrutinize the biotechnology company applying for insurance abroad. See Goudsmit, *supra*. Before approving a company's application, insurers should look at a company's experience, quality assurance practices, procedures, announced and credible intentions, evidence of good management practices, proper protocols and controls for researchers, relationships with clinical research organizations, claim history, and adequacy of informed consent

procedures and forms. *Id.* Therefore, the task of obtaining and providing sufficient insurance protection and risk management requires both biotechnology companies and their insurance carriers to evaluate each other carefully as well as the pros and cons of proceeding to an effective insurance contract.

C. The EU Clinical Trial Directive

U.S. biotechnology companies wishing to conduct clinical trials in the European Union must comply with uniform protocol in place there. In 2001, the EU enacted the Clinical Trial Directive, a uniform set of ethical and scientific quality requirements for human clinical trials. See Council Directive 2001/20, Clinical Trial Directive, 2001 O.J. (L 121) 1 (EC). The Directive mandates that EU members enact national legislation in compliance with the requirements. See <http://www3.imperial.ac.uk/clinicalresearchoffice/researchgovernance/eu-directives/>. Biotechnology companies conducting clinical trials in the EU should be aware of the Clinical Trial Directive requirements, as well as any additional requirements of each country. See Nicola Maguire & George Pickering, *Foreign Policy*, International Clinical Trials (2001), available at <http://www.samedanltd.com/homepage/ict/summer2006/NicolaM.pdf>.

Under the Directive, the sponsor of a clinical trial conducted in the EU must either be established in the EU, or appoint a resident of the EU as the sponsor's legal representative and qualified person to represent the research institution. *Id.* Additionally, the sponsor may not begin a clinical trial in the EU until the international ethics committee has approved the study. Clinical Trial Directive, *supra*, at art. 9.

It is also important to examine the individual regulations governing clinical trials in each nation in which they are conducted. Several countries in Europe mandate that a company provide compensation for injuries incurred during a clinical trial, such as requiring a company to pay participants who are injured on a no-fault basis. See Larry D. Scott, *Research-Related Injury: Problems and Solutions*, 31 J.L. Med. & Ethics 419, 424 (2003). The Directive contains stringent requirements for companies wishing to conduct clinical trials in the EU to ensure that "the interests of the patient always prevail over those of science and society." Clinical Trial Directive, *supra*, at art. 4.

D. Good Clinical Practice

The Clinical Trial Directive was enacted in an attempt to meet Good Clinical Practice (GCP), an international ethical and scientific quality standard that governs all components of a clinical trial involving human research subjects. See *Inspections – Good Clinical Practice*, European Medicines Agency, available at <http://www.emea.europa.eu/>. The Declaration of Helsinki, available at <http://www.cirp.org/library/ethics/helsinki/>, provided the basis for the GCP.

Compliance with GCP should assure that clinical trials are conducted ethically, adequate protection is provided to research subjects, and clinical trial data is credible. *Id.* The EU has adopted this standard, and unified standards have also been developed for the U.S. and Japan. *Id.* As new and potentially more stringent standards are adopted, biotechnology companies must be able to comply with them.

E. The French Law on Protection of Persons Undergoing Biomedical Research

Recently, several issues have been raised regarding the fairness and adequacy of the U.S. system for research and approval of a new drug or medical device. See Ivan Berlin & David A. Gorelick, *The French Law on "Protection of Persons Undergoing Biomedical Research": Implications for the U.S.*, 31 J.L. Med. & Ethics 434 (2003). These issues include: adequacy of the IRB system; remuneration of volunteers as possibly creating undue inducement to participate; compensating research subjects for health problems caused by clinical trials; and effective sanctions to discourage and punish violations of ethical standards governing human subject participants. *Id.*

French law governing human clinical trials serves as a good comparison for the alleged deficiencies of the U.S. guidelines. *Id.* The French Parliament passed the act entitled "Protection of Persons Undergoing Biomedical Research," commonly known as the Huriet Law, to protect participants in clinical trials, investigators, and sponsors of biotechnological research. Law No. 88-1138 of December 20, 1988, Journal Officiel de la Republique Francaise [J.O.] [Official Gazette of France], December 22, 1988, pp. 16,032-16,035. The law was designed to ensure that clinical research protocols are ethical and adequate. See Berlin & Gorelick, *supra*, at 434.

Several significant differences between the French and U.S. systems bear emphasis. *Id.* To begin, French law distinguishes between two categories of clinical research; biomedical research providing direct

benefit to the clinical participants, and all other types of research. *Id.* at 435. The U.S., however, does not. *Id.* In France, the research sponsor is financially responsible for any harm caused to research subjects during the trial, as well as to investigators for civil liability, which is paid with mandatory insurance coverage. *Id.* The United States presently requires no such coverage. The French regulations apply to all human research conducted in the country, while the U.S. system only applies to research supported or regulated by the federal government. *Id.* at 437. The French system uses local ethics committees appointed by the local government that have jurisdiction over a certain geographical area, while the U.S. committees (IRBs) are often part of the research institution, which may create a conflict of interest. *Id.*; see also Robert Gatter, *Conflicts of Interest in International Human Drug Research and the Insufficiencies of International Protections*, 32 Am. J.L. & Med. 351 (2006). Finally, France requires that ethics committees be tracked and submit protocols for review, while the U.S. has no such system in place. Berlin & Gorelick, *supra*, at 435.

F. The Issue of Extraterritorial Application of U.S. Laws and Regulations

Absent a clear international standard or explicit United States law, it is difficult for the U.S. to regulate the conduct of biotechnology companies conducting clinical trials abroad. See, e.g., *Microsoft Corp. v. AT&T Corp.*, 127 S. Ct. 1746, 1758 (2007) (holding that courts presume against extraterritoriality of U.S. law). The Supreme Court stated that even when a statute permits a specific extraterritorial application, the exception does not override the presumption and may be read narrowly. *Id.* This methodology applies even when such a narrow reading could create a loophole for parties seeking to evade liability. *Id.* at 1759 (holding extraterritoriality exception only covers copies of software actually dispatched from U.S., but not copies made abroad from master software disks supplied in the U.S.).

The Supreme Court has held that Congress unquestioningly has the authority to regulate the conduct of U.S. employers outside the territorial jurisdiction of the U.S. See, e.g., *Torrico v. IBM*, 213 F. Supp. 2d 390, 397 (internal citations omitted). However, courts will assume ordinarily that Congress has not exercised such authority unless it explicitly states its intent to reach acts performed in other countries. *Id.* This doctrine has led courts generally to reject a party's claim that a statute should be applied to a foreign locale.

For example, the Supreme Court previously interpreted Title VII of the Civil Rights Act of 1964 as not applying to the actions of U.S. employers to U.S. employees working abroad. *EEOC v. Arabian American Oil Co.*, 499 U.S. 244 (1991), *overruled by* The Civil Rights Act of 1991, 102 Pub. L. No. 166, § 109, 105 Stat. 1071 (1991). In *EEOC v. Arabian Oil Co.* (“Aramco”), the Court reasoned that Congress did not provide for overseas enforcement when it could have (indeed, when such a construction would have likely implemented the statutory purpose without creating a true conflict with the policy or interests of Saudi Arabia), so Title VII only applied domestically (even though such an interpretation undermined the statutory purpose without advancing any competing policy or interest of Saudi Arabia). 499 U.S. at 248. In an understandable and quick response, Congress passed the Civil Rights Act of 1991, which rejected the Supreme Court’s interpretation of Title VII in cases such as *EEOC v. Aramco*. See *Landgraf v. Usi Film Prods.*, 511 U.S. 244 (1994). Section 109 of the Act, titled “Protection of Extraterritorial Employment,” defined an employee for purposes of Title VII and the Americans with Disabilities Act as including an individual who is a citizen of the U.S. employed in a foreign country. 102 Pub. L. No. 166, § 109.

In amending Title VII to override *EEOC v. Aramco*, however, Congress, did not succeed in putting to rest the Supreme Court’s general presumption against extraterritoriality. And a few recent cases address the presumption in a careful and balanced way rather than woodenly. For example, *Hoffman-La Roch Ltd. V. Empagran S.A.*, 542 U.S. 155 (2004) (Breyer, J.), illustrates the care that the Supreme Court can take if it wishes in dealing with claims to apply domestic laws abroad. There, the Court declined to apply the Foreign Trade Antitrust Improvement Act (“FTAIA”) to price-fixing activity that had significant foreign effects but was independent of domestic effects. *Id.* at 164. The Court reasoned that it construes ambiguous statutes to avoid unreasonable interference with the sovereignty of foreign nations under applicable rules of statutory construction and consideration of foreign interests as well as domestic ones. *Id.* Additionally, the history of the FTAIA suggests that Congress intended to clarify or limit the Sherman Act, but not expand it to the extent sought by the claimants. *Id.* at 169.

Applying such interpretive approaches to the phenomenon of clinical trials conducted abroad, courts seem unlikely to find that current otherwise pertinent U.S. statutes reach conduct in foreign countries (that are independent nation states and not simply territories or possessions of the U.S.) unless such statutes contain specific language stating (or clearly implying in light of both their words and their purpose) that they are meant to apply abroad. Given this likely approach, and until a controlling

and countervailing court decision is handed down or a statutory amendment is enacted, the courts may hold that the FDA lacks sufficiently explicit authority to regulate the treatment overseas of human subjects in foreign clinical trials, or punish or otherwise sanction biotechnology companies for acting unethically in foreign countries, see DuBois, *supra*, at 193, although it may withhold approval in the U.S. of a human pharmaceutical or medical device that has not been tested according to its standards. See Basic HHS Policy for Protection of Human Research Subjects, 45 C.F.R. § 46 (2007); *but see* 45 C.F.R. § 46.101(h) (stating that when research takes place in foreign countries, a department head may substitute FDA regulations for foreign ones if it deems the foreign procedures to afford at least the same protections to human research subjects as would be provided under FDA regulations).

The inapplicability of U.S. law becomes particularly problematic when foreign drug trials are conducted for the purpose of avoiding U.S. government controls, such as the Johns Hopkins University School of Medicine trial in India of an anti-cancer drug banned by the FDA. See DuBois, *supra*, at 168, citing Office of Inspector General, Department of Health and Human Services, *The Globalization of Clinical Trials: A Growing Challenge in Protecting Human Subjects*, Sept. 2001, at 6, available at <http://oig.hhs.gov/oei/reports/oei-01-00-00190.pdf>. Therefore, ensuring that ethical protocols and adequate protections exist in international clinical trials presents a special challenge when, under presently controlling precedents governing the interpretation of U.S. statutes, the U.S. lacks authority to regulate or punish companies conducting experiments abroad and the company is not seeking FDA approval in the U.S. based on the foreign clinical trials.

G. Alien Torts Claims Act Issues, Including the Pfizer case and its Nigerian Clinical Trial

As the number of foreign clinical trials conducted in developing countries increase, so do calls for the U.S. to provide a forum to punish extraterritorial abuses in areas such as informed consent. Evans, *supra*, at 479; Erin Talati, *An Open Door to Ending Exploitation: Accountability for Violations of Informed Consent under The Alien Tort Statute*, 155 U. Pa. L. Rev. 231 (2006). Recently, attempts have been made to revive the Alien Torts Claims Act ("ATCA") as a potential way to reach U.S. biotechnology companies conducting allegedly abusive clinical trials abroad. See *Abdullahi v. Pfizer, Inc.*, No. 01 Civ. 8118, 2002 U.S. Dist. LEXIS 17436 (S.D.N.Y. Sept. 17, 2002), *vacated and remanded by* No. 02-9223, 2003 U.S. App. LEXIS 20704 (2d Cir. Oct. 8, 2003), *dismissed*

by No. 01 Civ. 8118, 2005 U.S. Dist. LEXIS 16126 (S.D.N.Y. Aug. 9, 2005).

A plaintiff bringing a claim under ATCA must prove three elements: the plaintiff is an alien to the U.S.; the defendant committed a tort; and the tort was committed in violation of the law of nations or a treaty of the United States. See 28 U.S.C. § 1350 (2007). The recent case of *Abdullahi v. Pfizer, Inc.*, is instructive on how U.S. courts may treat such claims.

In *Abdullahi v. Pfizer, Inc.*, Nigerian children were given an experimental drug administered by Pfizer meant to treat meningitis. 2002 U.S. Dist. LEXIS 17436, at *1. Several children who received the drug died and others suffered serious side effects. *Id.* at *6. Nigerian family members sued Pfizer under the ATCA, alleging violations of the Nuremberg code, the Declaration of Helsinki, the International Covenant on Civil and Political Rights, and customary international law. *Id.* at *1. The district court dismissed the case on the grounds of *forum non conveniens*, but the court of appeals vacated and remanded, holding that the court below should take notice of a similar case in Nigeria that had been dismissed. 2003 U.S. App. LEXIS 20704, at *7-10. On remand, the district court dismissed the claim for lack of subject matter jurisdiction, finding that the ATCA does not create a private cause of action. 2005 U.S. Dist. LEXIS 16126, at *1. The district court concluded that although non-consensual medical experimentation violates the law of nations, such a violation does not itself create a cause of action and it is up to Congress to decide whether and how to react to such violations. *Id.* at *25.

The district court also dismissed the plaintiffs' claim under the doctrine of *forum non conveniens*, finding Nigeria to be a more appropriate location to file suit. *Id.* at *2. The district court found insufficient evidence to support the plaintiffs' allegation that the Nigerian forum was inadequate because of corruption and bias. *Id.* at *45-47. However, the possibility of foreign government officials ignoring or condoning abuses committed by biotechnology (or other pharmaceutical) companies is very real, because third world governments often see clinical trials as the only way to obtain otherwise unaffordable medical treatment for their citizens. See Evans, *supra*, at 478. See also Gatter, *supra*, at 353.

In an interesting twist, the Nigerian government has recently brought suit against Pfizer in the United States for violations occurring during the 1996 meningitis clinical trial. See Joe Stephens, *Pfizer Faces Criminal Charges in Nigeria*, Wash. Post, May 30, 2007, at A10. The lawsuit alleges that researchers did not obtain informed consent before

conducting the trial, and gave the control group a dangerously low dose of a comparison drug. *Id.* The Nigerian government withdrew the civil lawsuit in July 2007, reportedly in order to file a new suit alleging fraud based on recently discovered material. Bashir Adigun, *Nigeria Plans New LawsUIT Against Pfizer*, Forbes.com, July 20, 2007, <http://www.forbes.com/feeds/ap/2007/07/20/ap3936157.html?partner=alerts>. Reporters called this move “a rare - - perhaps unprecedented - - instance in which the developing world’s anger at multinational drug companies has boiled over into criminal charges.” Joe Stephens, *supra*, at A10. However, if alien plaintiffs do not have recourse under U.S. statutes such as the ATCA, a suit brought by a foreign government may be the only way to enlist worldwide attention as well as sanction biotechnology companies for violations of local and international standards.

II. Tort Liability Issues

Tort liability is one area of exposure that has already confronted biotechnology companies, not only in risk management planning but also in litigation. Several tort liability theories potentially affecting them are outlined below.

A. Products Liability, including Failure to Warn

Historically, the outcomes of products liability lawsuits against pharmaceutical manufacturers have been difficult to predict. See Kim Copper, “High and Dry?” *The Public Readiness and Emergency Preparedness Act and Liability Protection for Pharmaceutical Manufacturers*, 40 J. Health L. 65, 82 (2007). Precisely because it is difficult to foresee the likelihood or possible outcomes of litigation in this area, clinical trials liability insurance is necessary to protect a company from possible litigation.

In some cases, FDA regulations governing warnings will preempt private litigation in this area. See *Reeves v. AcroMed Corp.*, 44 F.3d 300, 302 (5th Cir. 1995). In *Reeves v. AcroMed Corp.*, the plaintiff filed a claim against a medical device manufacturer for injuries allegedly caused by the device. *Id.* at 301. However, the appellate court found that the Medical Device Amendments (“MDAs”) to the FDA preempted the plaintiff’s products liability claim of failure to warn. *Id.* at 302. The court held that the MDAs establish an extensive enforcement scheme under which the FDA must police violations of its regulations, so the issue should not have been brought to the jury to second guess. *Id.* at 307.

So far, the biotechnology industry has been relatively safe from products liability lawsuits. As the number of human pharmaceuticals in distribution or in the pipeline for distribution to the public increases, however, it seems likely that products liability litigation may emerge. For anticipatory discussions, see Michael Traynor & Brian Cunningham, *Emerging Product Liability Issues in Biotechnology*, 3 High Tech. L. J. 149 (1989), and Michael Traynor & Eleanor Fox, *Biotechnology for Human Life and Health - The Special Case for a Negligence-Only Rule to Promote Critical Innovation*, 6 High Tech. L. J. 1 (1991); see also Michael Traynor, *Products Liability: The Reasonable Alternative Design Test, The Learned Intermediary Rule, and Recent Developments*, in ALI-ABA Course of Study Materials: United States Domestic and International Litigation and Dispute Resolution, April 2002.

B. Informed Consent, and Related Medical Malpractice Issues

Lawsuits based on human research subjects are on the rise, and most of the litigation so far has centered on the issue of informed consent. See Tooher, *supra*.

The recent Te Genero drug trial that nearly killed all six research subjects in England, most of them immigrants and unemployed, has caused British regulators to explore whether more stringent safeguards should be required when conducting "first in man" trials. Elizabeth Rosenthal, *British Rethinking Test Rules After Drug Trial Nearly Kills 6*, N.Y. Times, Apr. 8, 2006, at A1. Experts have also called into question the short length of time between testing the research subjects, which deviated from standard practice. *Id.* This widely publicized case could have far-reaching impacts on clinical trial regulations and lawsuits arising from failure to comply with clinical trial regulations.

Possible theories of litigation surrounding informed consent include: whether the investigator should have told terminally ill patients that the clinical trial was in the toxicity stage as opposed to the efficacy stage or more clearly and unequivocally informed them that they might die or suffer serious irreparable injury; whether the investigator told subjects the trial was a therapy as opposed to an experimental trial; whether researchers acted fraudulently by not revealing deaths of previous subjects to current volunteers; and whether the lead investigator acted fraudulently by not disclosing his financial ties to the sponsoring biotechnology company. *Id.* Several recent cases may also shed light on viable claims based on informed consent violations or medical malpractice.

In a claim for medical malpractice in the clinical trial setting, a central issue appears to be whether the researcher has a physician-patient relationship with the human research subject. *See, e.g., Clermont-Lundy ex rel. Lundy v. Zimbalist*, No. 4950/03, 2005 WL 3309753 (N.Y. Sup. Ct. Oct. 5, 2005). Most courts have found that no such relationship exists and subsequently dismissed a malpractice suit. In *Payette v. Rockefeller University*, plaintiff was asked to participate as a control person in an experimental diet study and was given a series of iodine injections as part of the program. 220 N.Y.S.2d 69, 70 (N.Y. App. 1996). When the plaintiff later experienced health problems, she sued the university for medical malpractice. *Id.* at 71. However, the trial court dismissed the claim as insufficient because she underwent procedures strictly as a volunteer of a study program, not as a patient with a medical condition. *Id.* at 72. Moreover, the plaintiff did not consult the university as a health care provider or undergo the injections as part of medical treatment. *Id.* By contrast, where a plaintiff seeks diagnosis or treatment of a medical condition from a research institution, such institution could be seen as providing health care services and therefore vulnerable to medical malpractice suits. *See Lundy v. Zimbalist*, 2005 WL 3309753, at *5. The line between medical treatment and voluntary study programs may become blurred when experimental drugs are given to patients suffering from a known medical condition for the purpose of curing or alleviating that condition. (It bears noting that the line between investigator and treating physician may also become relevant in determining whether the biotechnology company that is sponsoring a drug in a criminal trial has insurance coverage, or is required to give indemnity, or is entitled to indemnity, depending on the insurance policies and clinical trial contractual arrangements involved.)

Regardless of this distinction, courts have concluded that a research subject is not barred as a matter of law from bringing negligence actions against a research institution. In *Grimes v. Kennedy Krieger Institute, Inc.*, the Maryland Court of Appeals held that non-therapeutic scientific studies could still create special relationships, which would give rise to a duty of care between researcher and subject. 782 A.2d 807, 818 (Md. 2001). The Maryland court cited the Nuremberg Code as authority that researchers could be held liable for negligence even though there was no judicial precedent on the issue. *Id.* at 835. Participants in a clinical trial could therefore sue the research institution for failure to comply with the Nuremberg Code requirements, such as obtaining informed, voluntary consent. *Id.*

C. Negligence Per Se

Although rarely seen, a plaintiff may bring a claim of negligence per se when defendant's conduct in a clinical trial fell below the standard of care delineated in federal regulations. For example, in *Daum v. SpineCare Medical Group, Inc.*, the plaintiff did not see or sign a consent form to use an experimental spine device until the morning he was scheduled for surgery, and earlier consent forms did not mention that the device used would be experimental and used as part of a study to test its safety. 52 Cal. App. 4th 1285, 1298 (1997). After doctors discovered a deep bone infection caused by the device, the plaintiff sued and alleged negligence per se. *Id.* at 1299. The court held that federal regulations require a subject to be informed that the study involves research and be told which procedures are experimental, and failure to adhere to federal guidelines amounts to negligence per se. *Id.* at 1309-10 (citing 21 C.F.R. § 50.25(a)(1)). (On tort remedies for violation of statutes or regulations and the doctrine of negligence per se, see generally, Michael Traynor, *Public Sanctions, Private Liability, and Judicial Responsibility*, 36 Willamette L. Rev. 787 (2000).)

D. Fraud

Allegations based on fraud are relatively new in the clinical trial arena, but they may become more common over time. In 2001, families of patients enrolled in a melanoma study sued the research institution, IRB, and drug manufacturer for fraud, alleging failure to follow federal human subject regulations. See Tooher, *supra*. Although this case eventually settled in state court, it brings up an interesting new theory of liability. *Id.*

In addition to possible securities litigation (discussed below) arising from statements made by drug manufacturers, a plaintiff may also attempt to bring a claim of fraud for allegedly misleading the public by providing only positive information of results of a clinical trials. See Mark E. Nagle, *State "Fraud" Suits Over Drug Clinical Trial Results Tread on Free Speech Rights*, Wash. Legal. Found, Vol. 19, No. 30, Sept. 17, 2004. However, courts might not allow a claim of fraud against the public if the company made full disclosure to all regulatory agencies. *Id.* Additionally, if mandatory disclosure of all clinical trial results were required, there is a possibility that biotechnology companies would cut short trials that might be headed toward negative or inconclusive results. *Id.*

E. Other Tort Theories

In addition to strict liability and negligence actions, plaintiffs may invoke a claim of battery if they were used as research subjects without their knowledge or consent. See Mastroianni, *supra*, at 172-73. Other possible bases for lawsuits brought by research subjects include trespass, invasion of privacy, and breach of confidentiality. *Id.* at 193. As the number of individuals enrolled in clinical trials in the U.S. alone rose to 3.6 million in 2003, the possibility of new theories of litigation has correspondingly increased. See Tooher, *supra*.

III. Possible Emerging Contract Third Party Beneficiary Theory

Although there have been no reportedly successful claims thus far, at least one scholar has urged the viability of a breach of contract claim against a research institution. Lori A. Alvino, *Who's Watching the Watchdogs? Responding to the Erosion of Research Ethics by Enforcing Promises*, 103 Colum. L. Rev. 893, 919-20 (2003). Existing law may be involved by a claimant to support the theory of research subjects as third party beneficiaries to contracts of assurance between a federal sponsor of research and a research institution. *Id.* If the courts uphold this theory, then either party to the contract may be subject to liability to research subjects as third party beneficiaries for any subsequent breach.

IV. Possible Methods of Avoiding or Mitigating Exposure to Liability

With the possibility of various liability claims increasing, biotechnology companies and research sponsors should look for potential methods to mitigate or avoid exposure at all stages of a clinical trial.

A. Quality Assurance, including Monitoring During the Clinical Trial

Quality assurance is a familiar concept and applicable procedures should be followed through the development of a drug. One that deserves particular mention here is the subject of monitoring, not only of the clinical trial generally, but of the dosages administered, the time between doses, the subjects' reactions and symptoms, and other factors that bear or potentially bear on the risk that the subjects may die or suffer serious injury during the trial.

In 1993, the National Institutes of Health ("NIH") abruptly ended a clinical trial studying a new hepatitis B medication Fialuridine ("FIAU") after one of the patients was suddenly hospitalized with liver failure. Institute of Medicine, *Review of the Fialuridine (FIAU) Clinical Trials* 1

(Frederick J. Manning & Morton Swartz eds., 1995). Although each participant had taken the drug for eight weeks with reports of only mild side effects, the majority of participants later experienced serious health problems and five patients died. *Id.* As a result, the Secretary of the Department of Health and Human Services (“DHHS”) commissioned a study by the Institute of Medicine to analyze the FIAU clinical trials and determine whether any rules or procedures governing such trials need to be changed. *Id.* at 1-2.

After careful evaluation, the Institute of Medicine Committee (“IOMC”) found that sufficient justification existed to initiate the trial, that the protocol and consent form were adequate, and the conduct of the clinical trial met or exceeded the prevailing standard of care. *Id.* at 9. However, the IOMC and the FDA both recommended creating formal independent ongoing monitoring during clinical trials as well as designating comparison groups in all stages of testing. *Id.* at 11, 13. The IOMC and the FDA also agreed that longer follow up of clinical trials would be useful. *Id.* The IOMC detailed various recommendations in the areas of trial design, adverse event reporting, compliance audits, and further research into FIAU toxicity. *Id.* at 13-15.

B. Increased Monitoring by IRBs

After the highly publicized death of Jesse Gelsinger, a healthy young man who underwent experimental genetic therapy administered in a clinical trial, demands for IRB reform have increased. See Sharona Hoffman, *Continued Concern: Human Subject Protection, the Institutional Review Board, and Continuing Review*, 68 Tenn. L. Rev. 725, 725 (2001). Critics of the current IRB structure call the level of oversight of clinical trials highly inadequate. *Id.* See also Cinead R. Kubiak, *Conflicting Interests & Conflicting Laws: Re-Aligning the Purpose and Practice of Research Ethics Committees*, 30 Brook. J. Int’l L. 759 (2005). Currently, IRBs are not required to visit research sites, oversee the administration in the field of the informed consent process, or seek feedback from research subjects, and they may rarely do so. *Id.* at 726-27. Additionally, if one IRB does not approve a study, a biotechnology company might simply apply to another without making substantive changes. See John Abramson, *Guarding the human guinea pigs*, L.A. Times, Apr. 7, 2006, at B11. See also Valerie Junod, *Drug Marketing Exclusivity under United States and European Union Law*, 59 Food & Drug L.J. 479 (2004). In other countries, rigorous oversight from independent review boards is deemed essential in order to obtain meaningful continuing review. Abramson, *supra*, at 738-39.

A more active IRB could mitigate, or help avoid altogether, several potential problems in clinical trials. For example, continuing reviews and monitoring may identify research errors that would otherwise go undetected or lead to the early ending of unsuccessful trials or to their temporary suspension and to significant precautions and modifications when they allowed to resume. *See id.* at 741. Such reviews and attendant monitoring may also decrease the possibility of litigation associated with research risks. *Id.* at 743. Some proponents of an IRB transformation believe that on site monitoring would safeguard the welfare of research subjects by ensuring that the informed consent process is and remains valid. *Id.* at 757. Continuing review would thereby benefit physicians, medical facilities, research sponsors, and clinical trial participants. *Id.* at 748.

C. Compensation for Research-Related Injuries

Given the risks inherent in medical research, no-fault compensation for research-related injuries may be a favorable mode of protecting research subjects as well as biotechnology companies. Although the U.S. government's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research proposed an experiment to determine the need and costs of no-fault compensation for injured research subjects, one report, in 2003, indicated that no such experiment had then been conducted or reported on. Larry D. Scott, *Research-Related Injury: Problems and Solutions*, 31 J.L. Med. & Ethics 419, 419 (2003). However, the University of Washington has provided compensation for injury incurred during clinical trials on a no-fault basis since 1972, and several scholars agree that no-fault compensation has many favorable aspects. *Id.* at 420. This approach bears serious consideration in the U.S. as evolving ethical standards here as well as legal requirements in foreign countries call for it to be implemented. Although the empirical data is lacking, this approach might hold the promise of reducing the incidence of substantial tort liability claims and attendant increased liability insurance costs.

James Childress, professor at the University of Virginia's Center for Biomedical Ethics, has outlined three arguments in favor of no-fault compensation: the research subject accepts a risk that would not otherwise be encountered by agreeing to participate in the study; the activity benefits society; and the research may be sponsored or mandated by the U.S. government. *Id.* Childress argues that it is logical to assume that those standing to benefit from the outcome of the research would have a moral obligation to compensate an injured research subject. *Id.* at 423. Additionally, several countries in Europe

provide compensation on a no-fault basis for injuries incurred during a clinical trial. *Id.* As more clinical trials move abroad and international standards regarding clinical trials become more prevalent, the U.S. may also recognize the benefits of a no-fault compensation program.

D. The Possible Issue of a Physician Acting in the Dual Role of Treating Physician and Principal Investigator

This issue has arisen, as discussed above, in the context of medical malpractice actions against physicians. Whether and to what extent the dual capacity of an investigator/treating physician will be used to support a possible claim also against the sponsoring company or clinical research organization is a possible question that remains to be developed.

V. Insurance Issues

As previously noted, it is important for biotechnology companies conducting clinical trials to obtain liability insurance as part of a risk management strategy. (If indemnities are involved, a risk management program should include attention to contractual liability insurance as well as products liability and clinical trials insurance and errors and omissions coverage.) It is likewise important to understand the insurance application requirements in order to ensure that all aspects of clinical trial are covered. Merely obtaining an insurance policy may be insufficient.

A. Nondisclosure as a Ground for Rescission

Recently, a U.S. District Court in California allowed an insurer to rescind its insurance policy issued to a research institution because of a material misrepresentation made in the application. *Federal Ins. Co. v. Curon Medical, Inc.*, No. C-03-1356 VRW, 2004 U.S. Dist. LEXIS 22365, at *11 (N.D. Cal. Oct. 28, 2004). Curon Medical had entered into a clinical trial agreement to test an experimental medical device used to reduce the symptoms of fecal incontinence. *Id.* at *2-3. A trial participant was severely injured during the clinical trial, and one of the hospital physicians relayed to Curon's chief medical doctor that the research subject was consulting with an attorney. *Id.* at *3-4. Curon submitted an application to the Federal Insurance Company ("FIC") for a "claims made" insurance policy, but did not disclose the participant's injury as an incident that might reasonably be expected to give rise to a claim. *Id.* at *5. FIC issued Curon an insurance policy, and the research participant eventually filed a lawsuit against Curon. *Id.* at *6. FIC agreed to provide defense for the lawsuit subject to reservation of rights,

including the right to deny coverage based on Curon's failure to report the incident. *Id.* at *7.

After Curon and the participant settled, FIC initiated a lawsuit against the research institution. *Id.* at *8. The district court held that FIC was entitled to rescind its insurance policy issued to Curon for failure to disclose the participant injury incident. *Id.* at *10. The court reasoned that California law permits an insurer to rescind an insurance policy on the ground of the insured's material misrepresentation, and the failure to report the injury incident on the FIC application constituted such a misrepresentation. *Id.* at *10-11. Therefore, biotechnology companies seeking coverage of a clinical trial must diligently comply with all requirements of an insurance coverage application in order to prevent rescission.

B. Disclosure to Carrier in Connection with Reporting of Significant Adverse Events to the FDA

It is a realistic possibility that deaths and injuries will occur during a clinical trial. In general, and subject to analysis in particular situations, it may be good practice for the company to notify its insurance carrier if deaths or injuries occur and the company reports them to the FDA as a significant adverse event, even if an actual "claim" for purposes of a claims-made policy has not yet been made. The applicable policies will require examination to determine the requirements and provisions for reporting of a death or injury, for example, as an "occurrence" or, under some policies, as a "notice of circumstances" (see next paragraph). The reporting and notice requirements deserve particular attention because, for example, they bear on whether and under what policy coverage may be available if a claim is made, on provisions for "tail" coverage, and on disclosures to successor insurance carriers.

C. "Notice of Circumstances" under Certain Claims-Made Policies

The most commonly accepted form of insurance is written on a "claims made" basis, as opposed to an "occurrence" basis. See *Commerce Banc Insurance Services, supra*. A claim is covered in a "claims made" policy in effect at the time the claim is made, regardless of when the injury occurred, as long as the period of injury is included within the policy retroactive date. *Id.* By contrast, a claim is covered in an "occurrence" policy under the policy period in effect at the time of injury. *Id.* Some policies may provide for a "notice of circumstances" to alert the carrier to a situation that may eventuate in a claim.

D. Policy Condition of Compliance with FDA Protocol

Insurance carriers understandably do not wish to provide coverage to companies that deliberately disregard applicable FDA protocols. Some policies may provide a policy condition or exclusion under which coverage is not available if the company has not complied with such protocols. Plaintiffs, on the other hand, may allege noncompliance without realizing that such a pleading may present a coverage problem even if the company had in good faith attempted to comply with the protocols. A company presented with such a broad policy condition or exclusion may attempt to obtain an endorsement to the effect that good faith attempts to comply with applicable FDA protocols will not cause the condition or exclusion to apply (or some comparable endorsement) but there is no assurance that such a negotiation will be successful. It accordingly behooves companies and their counsel to examine carefully the policy conditions and exclusions.

VI. Securities Litigation and Class Action Issues: Recent Cases

Among the challenges facing biotechnology companies are whether, when and how it may be required to publicly disclose clinical trial results. Stockholders of a biotechnology company may sue the company for making material misrepresentations or omitting material problems arising during the course of a clinical trial. Additionally, a company may have a duty to correct or update its own previous disclosures. *See Backman v. Polaroid Corp.*, 910 F.2d 10 (1st Cir. 1990). State laws may also create a duty to disclose. *See, e.g.*, California Corporate Securities Law of 1968, § 25400(d). Disclosure and confidentiality are also important public policy issues. *See, e.g.*, Daniel R. Cahoy, *Medical Product Information Incentives and the Transparency Paradox*, 82 Ind. L.J. 623, 653-54 (2007) (discussing the proposed Fair Access to Clinical Trials Act ["FACT Act"] and Pharmaceutical Research and Manufacturers Accountability Act ["PHARMA Act"]). The cases below represent a variety of recent examples of securities cases brought against drug manufacturers (and they are cited briefly for illustrative purposes, not for extended analysis):

A. *In re Vaxgen*

In the case of *In re Vaxgen Securities Litigation*, plaintiff stockholders filed a class action lawsuit against Vaxgen for securities fraud. No. C 03-

1129 JSW, 2004 U.S. Dist. LEXIS 29812, at *2 (N.D. Cal. Apr. 14, 2004). Plaintiffs alleged that defendant drug manufacturers did not disclose the results of clinical trials indicating that their new vaccine was ineffective. *Id.* at *3. Plaintiffs bought stock during the class period, and once the manufacturer disclosed the results of the clinical trials, the stock fell 50 percent. *Id.* at *4.

B. *In re Entropin*

In re Entropin, Inc., Securities Litigation involves a class action claim made against Entropin for violating federal securities laws. No. CV 04-6180-RC, 2007 U.S. Dist. LEXIS 35157, at *4 (C.D. Cal. May 3 2007). Entropin conducted a Phase II clinical study of its sole drug, Esterom, to determine its efficacy. *Id.* at *7-8. Plaintiff stockholders filed suit against Esterom, claiming misrepresentations of the trial results, misleading statements regarding the efficacy of the drug, and failure to disclose that the study was unblind. *Id.* at *20-21.

C. *In re IntraBiotics Pharmaceuticals*

In re IntraBiotics Pharmaceuticals, Inc., Securities Litigation is a class action lawsuit filed by plaintiffs who purchased or acquired IntraBiotics stock during the class period. No. C 04-02675 JSW, 2006 WL 708594, at *1 (N.D. Cal. Mar. 14, 2006). Plaintiffs alleged that IntraBiotics secretly fixed the clinical trial data to indicate a positive trend in order to justify continuing the trial. *Id.* Plaintiffs further alleged that IntraBiotics made materially false and misleading statements regarding clinical trial results, and failed to comply with FDA protocol. *Id.* at *3-4, 6. However, the court found that plaintiffs had not pled sufficient facts to demonstrate falsity under the heightened pleadings standards of PLSRA. *Id.* at *9.

D. *In re Regeneron*

In the case of *In re Regeneron Pharmaceuticals, Inc., Securities Litigation*, plaintiffs filed a class action lawsuit against Regeneron for making materially false and misleading statements during the class period in which plaintiffs bought company stock. No. 03 Civ. 3111 RWS, 2005 WL 225288, at *1, 7-10 (S.D.N.Y. Feb. 1, 2005). Plaintiffs alleged that defendants made several public misrepresentations regarding an experimental new drug, including its effectiveness, lack of side-effects, reasons for pursuing its development, and the size of the market. *Id.* at *7-10. The district court held that plaintiffs had adequately pled sufficient facts under PLSRA and denied Regeneron's motion to dismiss.

VII. Public Policy Issues

As new drugs and vaccines become available, novel public policy issues take shape and gain attention. The list below highlights a few of the important issues that may affect biotechnology companies, research subjects, and the general public in the future.

A. Abigail Alliance and the Claimed Constitutional Right to Take Unproven Experimental Drug

When experimental drugs are tested on subjects with serious and debilitating diseases, the question arises as to what to do when a biotechnology company ceases testing the drug, but human subjects wish to continue receiving it. As more clinical trials today offer a high likelihood of benefiting research subjects themselves, participants have begun to assert a "right" to enter a study. See Mastroianni, *supra*, at 181. In 2003, the Abigail Alliance for Better Access to Developmental Drugs and the Washington Legal Foundation sued the FDA on the grounds that patients have a constitutional right to assume the risk of taking an unproven experimental drug. Karyn Hede, *Patient Group Seeks Overhaul of FDA Clinical Trial System in Court*, 98 J. Nat'l Cancer Inst., Sept. 20, 2006, at 1268. The D.C. Circuit Court of Appeals reversed the district court's dismissal of the claim in 2006, which has revived the plaintiffs' argument. *Id.*

Additionally, a group of individuals suffering from Parkinson's disease is suing Amgen for denying them continued access to an experimental drug. Tooher, *supra*. Amgen stopped testing its drug after determining that it may have potential side effects. *Id.* The patients based their legal argument on the right of individuals to be treated with dignity and cite the Nuremberg Code as supporting evidence. If a court should rule in favor of these individuals, it could revolutionize the types of clinical trials biotechnology companies are willing to undertake, informed consent requirements, and possible government involvement in clinical trials conducted by private institutions.

B. Underrepresentation of Women in Clinical Trials

Biotechnology companies could also face litigation for failure to include women in clinical studies for drugs that will eventually be marketed to women. See Institute of Medicine, *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, Vol. 2 (Anna C. Mastroianni, Ruth Faden, & Daniel Federman eds., 1999); Mastroianni,

supra, at 167, 182. It is well-recognized that men and women differ in physiological responses to treatment, so correspondingly it is important to include women in clinical studies of drugs that may be made available to them in the future. Mastroianni, *supra*, at 167. If a clinical trial does not include women, or includes insufficient numbers of them, such study may not provide meaningful or accurate information for disease treatment in women. *Id.*

One of the reasons women have been underrepresented in clinical trials is the fear of potential liability to the offspring of women who themselves are injured, as occurred in the DES lawsuits. *Id.* at 168. However, companies could be potentially held liable for negligence or strict liability if they conduct inadequate testing by excluding women from clinical trials. *Id.* at 182. Drug manufacturers could also be liable for defective design or failure to warn. See *Women and Health Research*, *supra*, at 94-95. As research in the HIV arena increases, the need to test and monitor women of a childbearing age will continue so as not to repeat the DES liability situation. See Mastroianni, *supra*, at 186.

C. Underrepresentation of Minorities in Clinical Trials

If there is a possibility that biotechnology companies and research institutions will be held liable for failure to include both genders in clinical trials, there is a good chance that these entities could also face litigation for failure to include minorities. In *Joseph v. Leavitt*, the plaintiff raised the argument that African Americans were systematically excluded from clinical trials. 465 F.3d 87, 93 (2d Cir. 2006). However, the Second Circuit deemed this argument waived because it was only raised at oral argument, and not before the district court or in any appellate brief. *Id.* at 93-94.

In the class action case *In re Viropharma, Inc., Securities Litigation*, the plaintiffs alleged that Viropharma made materially misleading statements regarding its clinical trials of the drug Pleconaril. No. 02-1627, 2003 U.S. Dist. LEXIS 5623, at *2 (E.D. Penn. Apr. 7, 2003). Plaintiffs claimed that Viropharma's Phase III study was extremely narrow because minorities and elderly were underrepresented, so its claim that Pleconaril was effective for all adults was a material misrepresentation. *Id.* at *10. The district court denied the defendant's motion to dismiss, finding that the plaintiffs' decision to buy Viropharma stock would be materially affected by the knowledge of the efficacy of the drug in general and in large subgroups. *Id.* at *33.

Exclusion of certain groups from clinical trials may become even more pertinent as U.S. biotechnology companies increasingly conduct their studies abroad. In an effort to ensure that foreign clinical trial data is accurate, and perhaps to avoid litigation, Japan has prohibited the use of foreign clinical trial data where immunological or ethnic differences exist between Japanese and non-Japanese. Katharine Neckers, *Harmonization of Drug and Medical Device Development in the US and Japan: Movement Towards International Cooperation in the Postgenomic Era*, 12 New Eng. J. Int'l & Comp. L. 295, 323 (2006).

D. Reduced Protection of Persons in Military Service

One group that does not receive the same protections and safeguards commonplace during clinical trials is the military. Federal courts have upheld the use of investigational drugs and vaccines on soldiers without their consent. Ashley R. Melson, *Bioterrorism, Biodefense and Biotechnology in the Military: A Comparative Analysis of Legal and Ethical Issues in Research, Development and Use of Biotechnological Products on American and British Soldiers*, 14 Alb. L.J. Sci. & Tech. 497, 503 n.25 (2004). The Department of Defense Directive ("DODD") allows waiver of consent requirements in a specific research project if it will "advance the development product necessary to armed forces . . . [that] may directly benefit the subject." *Id.* at 511. The military may also escape the consent requirement by classifying a new drug or vaccine as "use" rather than research under DODD 3216.2. *Id.* at 512. Additionally, the Supreme Court held that soldiers do not have a cause of action for injuries that "arise out of or are in the course of activity incident to service," which may include involvement in or use of investigational drugs. *Id.* at 518-19 (citing *United States v. Stanley*, 483 U.S. 669, 684 (1987)). The FDA has also recognized that informed consent may not be feasible in the combat context. *Id.* at 516.

E. Liability Shields Regarding Bioterrorism Countermeasures and Vaccines

Congress has recently taken steps to establish a no-fault compensation fund for certain limited circumstances. In an effort to encourage the development of new vaccine and bioterrorism countermeasures, Congress recently approved the Public Readiness and Emergency Preparedness Act ("PREPA"), which shields pharmaceutical manufacturers from liabilities for injuries caused during clinical trials of such drugs. See Copper, *supra*, at 65. PREPA creates a compensation fund to compensate eligible individuals injured by the use or

administration of these drugs, although the source of this funding is unclear. *Id.* at 68-69.

Those in favor of liability protection argue that biotechnology companies would refuse to enter the vaccine market if they were not shielded from liability. *Id.* at 78. However, others argue that liability protection will not keep drug companies in the market anyway, and liability protection is not seen as a major concern. *Id.* at 85.

In addition to PREPA, Congress proposed the Biological, Chemical, and Radiological Weapons Countermeasures Research Act in 2002, which provides biotechnology companies engaged in countermeasures with liability protection as an incentive to develop such products. Melson, *supra*, at 519-20. The effectiveness of such initiatives depends on adequate financial support of the compensation funds.

F. Freedom of Information and Confidentiality of Clinical Trial Data

In *Public Citizen Health Research Group v. FDA*, Public Citizen filed a Freedom of Information Act ("FOIA") request with the FDA asking it to release documents relating to drug applications that had been abandoned for health or safety reasons. 185 F.3d 898, 901 (D.C. Cir. 1999). The FDA refused to disclose information regarding discontinued pre-clinical and clinical studies, claiming the search was unduly burdensome. *Id.* at 901. Public Citizen filed a claim against FDA demanding the documents, and the district court denied FDA's motion to dismiss. *Id.* At the appellate level, FDA and an intervening drug manufacturer argued that any agency may withhold data under Exemption 4 of the FOIA. *Id.* The appellate court agreed, and held that the FDA was not required to disclose such documents. *Id.* See also Cahoy, *supra*.