Emerging Litigation Involving Human Research Subjects

A FUTURE FOR CLASS ACTIONS?

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Human subjects of clinical research are increasingly suing the pharmaceutical and medical device companies, research institutions, and individuals who conducted the research. Recent litigation has even named review board members and patient advocates as defendants. The claims range from negligence, lack of informed consent, and fraud to more novel theories, such as violation of a constitutional right to be treated with dignity. Plaintiffs attorneys often seek class action certification, with potentially significant implications for medical and scientific research. This article discusses the law affecting clinical research, the alleged problems with the current regulatory system, the role litigation has played in attempting to remedy these issues, and the outcomes of class action lawsuits involving human research subjects.

Laws Affecting Human Clinical Trials

A brief history. Before 1974, no federal statutes or regulations had been specifically designed to protect human participants in clinical research. A few federal departments—including the Central Intelligence Agency and various military branches—did have internal policies that set voluntary guidelines for their own research.[1] Furthermore, at the international level, the 1949 Nuremberg Code and the 1964 Declaration of Helsinki had attempted to establish worldwide ethical principles to be followed in medical research conducted on humans.[2] Although none of these guidelines constituted binding law in the United States, they formed the foundation for future federal regulations and are often cited by lawyers and some courts as the ethical standards by which research should be measured.[3]

In 1974, the Department of Health, Education and Welfare promulgated its first regulations intended to protect human subjects of research it funded. It began by mandating that institutions convene institutional review boards (IRBs) to review and approve research studies. That same year Congress passed the National Research Act,[4] which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The commission's mission was to make recommendations regarding the regulation of research funded by the Department of Health, Education and Welfare.[5] In 1979, the commission published its recommendations, called the Belmont Report, as a "statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects."[6] The Belmont Report provided three general guidelines still applicable to today's medical research: respect for person, beneficence, and justice. In regulatory parlance, these principles translate into informed consent, risk/benefit analysis, and fair subject selection criteria.[7]

In 1981, the Department of Health and Human Services (DHHS), which emerged from the split of the Department of Health, Education and Welfare into the Department of Education and the DHHS, and which subsequently took over the responsibility of regulating human research, used the national commission's recommendations to amend the 1974 regulations and to develop the first comprehensive federal regulations intended to protect human subjects. This set of regulations, entitled the Federal Policy for the Protection of Human Subjects, applied only to research conducted or funded by DHHS.[8] That same year, the Food and Drug Administration (FDA) also promulgated regulations, modeled on those of the DHHS, that were applicable only to clinical research connected to applications for a new

drug, medical device, or biologic.[9]

Also in 1981, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research recommended that all federal agencies conducting or funding human research adopt the DHHS regulations. This recommendation was implemented ten years later when 16 other federal agencies formally adopted the DHHS regulations, which became known as the "common rule."[10] This common rule does not apply to all clinical research in the United States. Instead, it applies only to research conducted or funded by any of the 17 signatory agencies. The rule also governs research at institutions that have contractually agreed through a federal wide assurance (FWA) to apply the regulations to all research they conduct, even if it is privately funded.[11] Currently, the Office for Human Research Protections (OHRP) of the DHHS is responsible for enforcing the common rule regulations. The FDA's human research regulations still exist as stand-alone regulations, separate from the common rule, and are enforced by the FDA's enforcement office.[12]

The common rule regulations fall into two main categories: the responsibilities of IRBs and the informed consent process. In addition, FDA and Public Health Service (PHS) regulations require the disclosure of researchers' financial conflicts of interest. These three areas are almost always the subject of lawsuits brought by human research subjects. Accordingly, we discuss them in detail.

Institutional review boards. IRBs have been delegated the initial responsibility for reviewing, approving, and monitoring all clinical research governed by the common rule and FDA-PHS regulations. Each IRB must have at least five members with sufficient training and experience to review and approve proposed research in accordance with federal regulations and internal policies. At least one member must have scientific expertise, at least one must have expertise in nonscientific areas, and at least one must have no affiliation to the research institution. No IRB member may approve or monitor a research study in which he or she has a conflicting interest.[13]

Before any research study is conducted, the IRB must approve the protocol and the informed consent documents.[14] The common rule requires IRBs to examine the potential benefits and anticipated risks of research, and to approve it only if satisfied that the risks have been minimized and are reasonable in relation to the benefits. The IRB also must review and approve the informed consent materials to ensure they contain the information required by the common rule.[15]

The IRB must conduct at least an annual review of the study,[16] in which it must evaluate whether any changes to the protocol or informed consent materials are necessary and ensure that adverse event reports are communicated to the appropriate governmental agency.[17] IRBs must keep detailed records of their activities, meetings, policies, and correspondence with researchers.[18]

Informed consent. Under the common rule, clinical researchers bear the responsibility for obtaining informed consent from participants and must do so in a noncoercive manner, providing the subjects with sufficient time and opportunity to consider whether to participate. The regulations specify what types of information must be disclosed and require that it be conveyed in understandable language. Required disclosures include that the person is enrolling in a research study; the purposes of the research; the procedures involved, and whether they are experimental; any reasonably foreseeable risks or discomforts; any anticipated benefits to the person; and alternative treatments and procedures available to the person.[19]

Conflicts of interest. One of the biggest concerns in clinical trials is the disclosure and management of researchers' financial conflicts of interests. Researchers typically receive compensation, often from sponsoring commercial entities. This is usually not problematic. However, when researchers have financial or proprietary interests in the drug or device being studied, or in the sponsor, a risk exists that the financial interests could adversely impact how the study is conducted.[20]

Only the PHS and FDA regulations currently require researchers to disclose conflicts of interest.[21] The PHS regulations, applicable to research funded by the agency or

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any of its departments (such as the National Institutes of Health), require a researcher to disclose to an IRB all "significant financial interests" he or she holds in the sponsor company or the product being researched if the financial interests would "reasonably appear to be affected by the research."[22] A "significant" financial interest is defined as greater than $10,000 per year or more than 5 percent ownership.[23]

FDA regulations do not impose any reporting requirements on clinical investigators.[24] Instead, the sponsor company is obligated to disclose: (1) any financial arrangements between it and the researcher greater than $25,000, (2) any property or financial interests the investigator holds in the tested product, and (3) any property or financial interest the investigator holds in the sponsor company greater than $50,000.[25]

Aside from these reporting requirements, no laws or regulations currently bar a researcher from conducting research due to a conflict of interest. Instead, conflict of interest determination lies solely in the discretion of the overseeing IRB. Moreover, no specific requirements demand that conflicts be disclosed to the study subjects.

Institutions that host clinical research trials may also be affected by financial conflicts of interest. Many hospitals and universities invest in the biotechnology sector, so instances may arise where a hosting institution has a financial or proprietary interest in the sponsoring company or the product being researched. Commentators have noted that clinical research is a large source of income for many medical institutions. Others fear that members of an institution's IRB, who are aware of the financial benefits of hosting research, may be adversely affected in their review and approval of questionable study protocols.[26]

Just as with researchers, no federal laws or regulations currently require research institutions to disclose, evaluate, or manage any financial conflicts of interest they may have in research conducted at their facilities.

Recent regulatory developments. On June 26, 2006, the FDA announced a new initiative—the Human Subject Protection and Bioresearch Monitoring Initiative—to modernize the regulation of clinical trials and bioresearch monitoring in order to protect human subjects and the integrity of clinical trial data. This initiative will analyze recent evolutions in the clinical trial process and develop regulations and compliance programs. To date, the initiative has developed guidance documents for industry and sponsors that include additional safeguards for children in clinical investigations and the establishment and operation of clinical trial data monitoring committees.[27]

Litigation Involving Human Research Subjects

Over the last five years or so, various federal committees and private organizations have identified areas needing improvement in human research trials. Plaintiffs lawyers have taken what they feel is the next logical step: filing lawsuits, including class actions, on behalf of subjects against researchers, institutions, and commercial sponsors. Although litigation involving human research participants is not entirely new, up until the late 1990s these lawsuits usually involved egregious conduct, such as where participants were never advised they were participating in medical or scientific research. Although lawsuits still make allegations of egregious conduct, many merely claim that the informed consent documents did not contain every piece of information a participant might want to know or that a researcher's financial interest influenced the way in which the study was conducted. Below we review the significant critiques of the current regulatory system and how they have formed the basis for plaintiffs' legal claims.

Concerns with the system. Between 1998 and 2001, both the DHHS Office of the Inspector General and the President's National Bioethics Advisory Commission issued reports highly critical of the IRB and federal oversight system.[28] The DHHS report concluded that the nation's 3,500 to 5,000 IRBs were not adequately performing their obligations because of enormous workloads and insufficient staffing, funding, training, and experience. It determined that improvements were possible in the disclosure and management of conflicts of interest and made various recommendations. In an April 2000 follow-up report, the inspector general's office found that only minimal progress had been made to correct IRB deficiencies.[29]

The president's commission report reached similar conclusions. It also recommended an overhaul of the regulatory framework, including discarding the common rule regulations and creating a centralized National Office of Human Research Oversight to supervise all federal and privately funded human research.[30] To date, this has not occurred.

The potential problems posed by conflicts of interest are a subject of

great debate. The biggest fear is not that researchers are, in fact, compromising the health of human subjects to further their financial interest but that the public may have such a perception. In 2001, both the Association of American Universities[31] and the Association of American Medical Colleges[32] published reports recommending that universities and institutions take steps to evaluate their policies and procedures for evaluating and managing conflicts of interest potentially affecting human research. On March 31, 2003, the DHHS published a draft guidance document in the *Federal Register* that attempts to provide institutions, IRBs, and clinical investigators with recommendations for identifying, evaluating, and managing financial conflicts of interest.[33]

The impact of human research subject litigation. Allegations of researcher misconduct, IRB deficiencies, and conflicts of interests—often based on concerns expressed in the government reports discussed above—are finding their way into filed complaints, with plaintiffs attorneys maintaining that litigation is a proper mechanism to force change.[34]

One very publicized example is the case of Jessie Gelsinger. As alleged in the complaint, Gelsinger was an 18-year-old with a mild form of a genetic disease called OTC, which affected his liver's ability to process ammonia. Researchers at the Institute for Human Gene Therapy at the University of Pennsylvania were studying whether a particular virus was an effective method of transferring healthy OTC genes to afflicted patients. Gelsinger enrolled in this study and subsequently died from complications caused by the virus being injected into his body to effectuate the gene transfer.

Gelsinger's family filed suit against the hospital that hosted the study, the hospital that reviewed and approved the study, the company that sponsored the research, the physicians involved in running the study, and a physician who consulted with the hospital to determine whether the study was ethical. The complaint alleged causes of action for assault and battery, lack of informed consent, intentional infliction of emotional distress, fraud and misrepresentation, fraud on the FDA, and strict products liability.[35]

The plaintiffs asserted that the study should not have been approved by the IRB because the risks greatly outweighed any potential benefits, arguing that no one expected Gelsinger to receive any therapeutic benefits while the potential risks were life-threatening. Given this risk/benefit ratio, the plaintiffs contended, the study as designed was unethical under federal and state law.[36]

The plaintiffs also asserted that the study should not have been performed because the lead investigator, Dr. James Wilson, had a conflict of interest that prompted him to run the study in a hazardous manner. Specifically, it was alleged that Wilson held significant financial and ownership interests in Genovo, the company that owned the virus being studied, and accordingly would profit if the study was successful.

Finally, the complaint alleged lack of informed consent, stating that Gelsinger was not fully informed of the risks, including that previous human subjects had suffered adverse effects and animal subjects had died. The lawsuit was settled for an undisclosed sum.[37]

This case demonstrates how plaintiffs attorneys are using the legal system to force changes in the way clinical research is conducted. Gelsinger's complaint alleged IRB deficiencies (approving an overly risky study), informed consent deficiencies, and a financial conflict of interest. More and more lawsuits are being filed against researchers, institutions, and sponsors alleging negligence, lack of informed consent, fraud and misrepresentation, violations of federal regulations, and breaches of the controversial right to be treated with dignity. These kinds of claims have been asserted in well-publicized lawsuits alleging IRB misconduct in a melanoma vaccine study (*McGee v. Robertson*[38]), involving allegedly improper lead abatement studies (*Grimes v. Kennedy Krieger Institute*[39]), and alleging informed consent deficiencies by a patient who received an experimental heart transplant (*Quinn v. Abiomed*[40]).

Class Actions

Using class action lawsuits in mass tort litigation has always been controversial. Although they have been permitted in both the state and federal court systems, recent changes in federal law have made it easier for class actions to be litigated in federal court. Traditionally, federal courts have been extremely reluctant to certify classes for mass tort claims because most tort cases are driven by individualized issues.[41] However, there seems to be a shift in the latitude some courts are willing to give plaintiffs who bring human research subject cases as class actions.

Class action lawsuits are favored by plaintiffs attorneys for several reasons: they enable hun-

dreds or thousands of individual claims to be brought in a single lawsuit; the focus tends to be on the defendants' conduct rather than on the individual plaintiffs, their injuries, and the strengths or weaknesses of their individual cases; plaintiffs attorneys can easily represent an entire class of plaintiffs and collect large damages and fees; and most class actions settle because defendants are exposed to significant financial and public pressure. Because all of these factors are often present in human subject lawsuits, it is no surprise that many are being brought in the form of class actions.

The Federal Rules of Civil Procedure and most state court rules delineate requirements that must be met before a case may be certified and tried as a class action. Under federal Rule 23, the court must undergo a two-step analysis before it may certify a proposed class action. Initially, the court must find that the four prerequisites of Rule 23(a) have been met:

1. the proposed class is so numerous that joinder of all members is impracticable [numerosity],
2. there are questions of law or fact common to the class [commonality],
3. the claims or defenses of the representative parties are typical of the claims or defenses of the class [typicality], and
4. the representative parties will fairly and adequately protect the interests of the class [adequacy of representation].[42]

The numerosity requirement focuses on the number of proposed class members. Courts have certified classes with as few as 13 members and denied certification of classes with as many as 300 members.[43] In most mass tort cases, the numerosity requirement is generally not a major obstacle.[44]

The commonality requirement is satisfied where the claims of the named plaintiff and the proposed class share at least one common question of law or fact,[45] for example, where they were injured by the same negligent conduct or defective product. Because commonality only needs to be shown as to one significant legal or factual question, courts often find this prerequisite satisfied.[46] This factor should not be confused with the further requirement under Rule 23(b)(3) that certification be granted only if common issues predominate over individualized ones.[47] That standard is discussed below.

Typicality is established when the claims of the named plaintiff and those of the proposed class members are sufficiently aligned because they arise from the same conduct or course of events.[48] This factor also requires that the class members assert claims, legal theories, and/or seek remedial relief reasonably similar to those asserted by the named plaintiff.[49] It sometimes poses problems for plaintiffs if the defendant's conduct differed as to some plaintiffs, such as where the alleged misconduct or defective product changed over time.[50] Most courts are willing to find that the named plaintiffs' interests are sufficiently aligned with those of the proposed class.

The last requirement focuses on whether the named plaintiffs and their counsel will fairly and adequately represent the interests of the proposed class members.[51] Adequacy of representation typically is not an issue.

If the requirements of Rule 23(a) have been met, the court must further find that the class action can be maintained in one of the three specific categories set forth in Rule 23(b):

1. prosecution of separate actions by individual members of the class would create a risk of (a) inconsistent or varying adjudications that would establish incompatible standards of conduct for the party opposing the class; or (b) adjudications with respect to individual members of the class that would be dispositive of the interests of the other members not parties to the adjudications or substantially impair or impede their ability to protect their interests;
2. the party opposing the class has acted on grounds generally applicable to the class, thereby making appropriate final injunctive or declaratory relief with respect to the class as a whole; or
3. questions of law or fact common to the members of the class predominate over any questions affecting only individual members and that a class action is superior to other available methods for the fair and efficient adjudication of the controversy.[52]

Mass tort plaintiffs usually seek certification under Rule 23(b)(3). As explained earlier, however, every tort case involves individualized issues, especially in the area of causation and damages. With mass

tort class actions, plaintiffs attorneys face the hardest challenge proving that common issues predominate over individualized issues.[53] This predominance standard is much more demanding than the commonality standard under Rule 23(a).[54] Class certification should be denied where significant issues of fact must be litigated on an individual basis to establish the defendants' liability.[55]

Rule 23(b)(3) also requires plaintiffs to show that a class action is superior in terms of fairly and efficiently managing the litigation. Courts generally find that no matter how many liability issues can be adjudicated on a classwide basis, every plaintiff's claim still must be individually adjudicated to resolve the action. Where a proposed class action will still require litigation of individual claims, most courts find that a class action will be too burdensome to manage.[56]

Increasingly, plaintiffs are relying on Rule 23(b)(2) as a basis for class certification, especially in cases where they seek relief in the form of medical monitoring. Although the issue is hotly disputed, most courts have found that a claim for a medical monitoring fund or program is a form of equitable relief.[57] For plaintiffs to rely on Rule 23(b)(2), the court must find that they are seeking predominately injunctive relief rather than money damages.[58] Where plaintiffs are seeking significant monetary damages as their primary relief, courts will not certify a class under Rule 23(b)(2).[59]

Class Certification Decisions

Diaz v. Hillsborough County Hospital Authority. One of the first class actions[60] filed by human subject participants was brought in 1990 by participants in a study intended to determine whether a combination of drugs would improve lung development in fetuses at risk of being delivered prematurely. The plaintiffs did not allege that they or their fetuses had been injured by the treatment. In fact, some of the fetuses may have benefited from the experimental treatment.[61] Instead, the complaint asserted that the informed consent process was so fundamentally flawed that no informed consent could have been given, and that the defendants' conduct violated the participants' constitutional right to be treated with dignity.[62]

The district court certified a class consisting of all pregnant women subjected to the defendants' treatment without informed consent. The court considered, first, whether the plaintiffs satisfied the four prerequisites of Rule 23(a), particularly whether sufficient commonality and typicality had been established. A critical issue in the case concerned the informed consent procedures. Although noting that individualized issues existed as to what each participant was told, the court found that the essence of the allegations concerning the informed consent policies and procedures affected all of the proposed class members. Moreover, the plaintiffs also met the typicality requirement because their claims all arose from the same treatment and informed consent practice.[63]

Having found that the four prerequisites of Rule 23(a) had been established, the court then considered whether the proposed class action fell into one of the categories provided for in Rule 23(b). It concluded that certification could be made pursuant to Rules 23(b)(2) and 23(b)(3). Under Rule 23(b), the court held that the defendants acted on grounds equally applicable to the class because the proposed class members were subjected to the same informed consent process. Reliance on Rule 23(b)(2) was proper because plaintiffs were seeking injunctive relief in the form of changes to the defendants' policies and procedures for protecting research participants. The court also certified the class under Rule 23(b)(3) based on its finding that the common issue of the informed consent procedures predominated over any individual issues such as plaintiffs' reliance or damages. Without much analysis, the court further found that a class action was the superior method of adjudicating the claims. Accordingly, the court certified a hybrid Rule 23(b)(2) class whereby liability was to be decided in the first stage pursuant to Rule 23(b)(2) procedures and damages would be resolved in the second stage using the "opt out" procedures of Rule 23(b)(3).[64]

The case settled. The court approved an agreement that provided class members a shared $3.8 million settlement fund and required the defendants to take specific steps to improve their protocol and informed consent process in future clinical trials.[65]

One may dispute whether the court correctly applied Rule 23(b) to this case. With respect to Rule 23(b)(3), the court correctly pointed out that in a typical informed consent case individual issues exist as to what each plaintiff was told and whether the lack of disclosure was a proximate cause of each plaintiff's injury. This case, however, may have concerned an informed consent process so deficient that the participants may not even have been aware they were

involved in a research experiment. The court, however, did not apply the more demanding predominance standard of Rule 23(b)(3), relying instead solely on its finding that the defendants' informed consent policy and process was a significant common issue that existed as to each plaintiff.

Certification under Rule 23(b)(2) was even more tenuous. Although the plaintiffs did assert a claim for injunctive relief, the amount of the settlement strongly suggests that their primary interest was monetary. At the time it certified the class, however, it is not clear whether the court was aware that plaintiffs were seeking significant monetary damages.

In re Cincinnati Radiation Litigation. This case involved radiation experiments conducted in the 1960s on participants with cancer to test the effects of varying levels of radiation on humans. Although the participants were told that they would be receiving radiation treatment for their cancer, in actuality the study had no therapeutic value.[66]

Suit was filed in 1994. In 1997, the parties reached a settlement agreement providing a monetary award and injunctive relief. The parties jointly moved for approval of the settlement and certification of the proposed class. The court denied the motion. It relied primarily on its finding that the prerequisites of commonality and typicality had not been satisfied because the claims were based on the lack of informed consent and the defendants' informed consent process had changed over the course of the study. As a result, individual issues as to what each plaintiff was told about the experiment predominated over any common issues. The court also denied certification under Rule 23(b)(2) although plaintiffs sought injunctive relief (the acceptance of a memorial plaque by the university) because the court felt that equitable relief was not significant to most members of the proposed class.[67]

In 1999, the court approved a new settlement agreement and certified the class initially proposed. Without much analysis, the court found that the four prerequisites of numerosity, commonality, typicality, and adequacy of representation had been established. In considering the type of class that it would certify under Rule 23(b), the court decided that a hybrid class under Rules 23(b)(2) and 23(d)(2), with notice and opt out provisions, was the most appropriate and fair. The court was swayed by the fact that the class members who had chosen to opt out had reached individual settlement agreements with the defendants.[68]

This case presented an egregious situation where persons were experimented on without their knowledge. In such extreme cases, the common conduct of the defendants rather than any individualized issues of informed consent and causation seems likely to be the chief factor in establishing liability.

Craft v. Vanderbilt University. This class action involved experiments conducted at Vanderbilt University from 1945 to 1947, with follow-up studies in the 1960s, to study the effects of radioactive iron on pregnant women and the children they delivered. In the complaint filed in 1994,[69] the plaintiffs asserted lack of informed consent, alleging that they were given dosages of radioactive iron without being told what they were ingesting and without knowledge that they were part of a scientific experiment. Some of the plaintiffs claimed they suffered injuries from the experiment and sought monetary damages; others claimed they were at an increased risk of future harm and sought medical monitoring relief.

The court certified two of the four proposed classes: one consisting of women who were subjects in the study, and one consisting of the women's children who were fetuses at the time. Analyzing the four prerequisites of Rule 23(a), the court found that the plaintiffs met the numerosity requirement because each proposed class consisted of several hundred plaintiffs and the commonality and typicality requirements because all of the proposed class members had been part of the same experiment. Although the court recognized that each proposed class member had individualized issues concerning how much of the radioactive iron they had ingested and how they were injured or at risk for injury, it found that the common issue of whether they had been informed of the study predominated, was critical to determining the defendants' liability, and could be decided on a classwide basis.[70]

The court certified two of the proposed classes under Rule 23(b)(2) because the defendants acted equally toward each proposed class member and the plaintiffs' request for medical monitoring qualified as injunctive relief that was appropriate for the entire class as a whole. The court found that the proposed classes could also be maintained under Rule 23(b)(3) because the common issues on liability, which involved the same experiment conducted by the same defendants and the same allegations of mis-

conduct, predominated over any individualized questions of exposure and damages.[71] The case was eventually settled for an undisclosed amount.

As in *Cincinnati Radiation*, the court in this case based its predominance finding on the egregious nature of the defendants' conduct, which amounted to experimentation without any consent. In such cases, courts seem more willing to find that the common issues of the defendants' conduct predominate over individualized issues such as causation and damages. Additionally, here a primary aspect of the plaintiffs' requested remedy was injunctive relief in the form of medical monitoring. When injunctive relief is a primary aspect of the relief sought, courts may be more willing to certify a class under Rule 23(b)(2) because in most cases the plaintiffs were subjected to the same clinical study, thereby allowing the court to find that the defendants acted on grounds generally applicable to the entire class.

Wright v. Fred Hutchinson Cancer Research Center. This class action involved a clinical trial conducted at the Fred Hutchinson Cancer Center in Washington to test the theory that the depletion of T-cells in donor bone marrow can reduce the risk of graft-versus-host disease following bone marrow transplantation. Trials were run from 1981 to 1993, during which time the protocol was changed approximately 10 times, including several changes to the informed consent forms.

Suit was brought in 2001, alleging that the researchers failed to disclose material risks, failed to reveal alternative treatments that were available, and failed to follow IRB recommendations. The lawsuit also alleged that the researchers and the institution had substantial conflicts of interest involving large payments, contracts, and ownership interests in the sponsoring company.[72] Certification was sought for three separate classes: (1) a class of all decedent participants, (2) a class of family members of the decedent participants, and (3) a class of the bone marrow donors of the decedent participants.

The court denied certification.[73] Although it found that the 80 plaintiffs satisfied the numerosity requirement and that the common questions (including whether there was a sufficient basis for the IRB to approve the study and whether conflicts of interest precluded a finding of informed consent) satisfied the commonality requirement, certification failed on the issue of typicality. None of the named plaintiffs were found to be typical of any of the three proposed classes. The participants had different prognoses and expectations, received individualized consent consultations, participated in any one of 10 different trials, and suffered individualized damages.[74]

The plaintiffs had relied on Rule 23(b)(3), but the court found that the number of individual issues affecting liability outweighed any common issues. For example, claims such as fraud and informed consent raised issues of what each individual plaintiff was told and what each relied on in consenting. These numerous individual issues made it difficult for the court to find that a class action was a superior method of adjudicating the claims.[75]

In November 2002, the district court dismissed the federal claims and remanded the case to Washington state court, where the remaining claims are still pending.[76]

This case highlights one of the obstacles plaintiffs face in obtaining class action certification in clinical research cases: clinical studies and informed consent information often change over the course of a study. The court's ruling that the typicality and predominance requirements had not been met was based on its finding that each proposed class member was not subjected to the same experiment and informed consent information.

Steubing v. Kornak. This proposed class action involves experimental cancer treatments conducted at the Stratton Veterans Administration Medical Center from 1999 to 2003. The suit was brought on behalf of Carl Steubing, a study participant who died during the course of the experimental treatment, and approximately 100 putative class members. The complaint names the two physicians who led the research and asserts causes of action for breaches of the right of dignity and bodily integrity, violations of federal regulations, and failure to obtain informed consent.[77] Since the initial filing, several other plaintiffs claiming injuries from the study have filed individual complaints.

The allegations, many of which have been substantiated by FDA and Veterans Administration investigations, state that the researchers altered participants' medical records, concealed patient histories, and failed to run necessary tests to avoid subject selection criteria. According to the FDA, at least one and possibly four subjects died as a result of the researchers' violations.[78] According to the complaint, one of the researchers hired by the medical center, Dr. Paul

Kornak, had had his medical license revoked in two states and had been convicted of mail fraud.[79]

The claims are still pending against the two researchers. Whether plaintiffs will seek to certify this case as a class action, and whether a certification motion will be successful, is unclear at this point.

Analysis and Implications

Plaintiffs counsel seeking class certification for suits involving human research participants face the same challenges as in other mass tort cases: There are often so many critical, individualized issues requiring resolution that courts will refuse class action treatment. For example, most human research cases involve claims of failure to obtain informed consent. The difficulty lies in that not every participant is given the same information about the research. Although all researchers provide written informed consent forms to all participants, there are also individualized verbal aspects of the informed consent process between the participants and the researcher, and between the participants and their own physicians. The issue of causation in informed consent cases is also an individualized issue.

In addition, as shown in *Wright* and the initial *Cincinnati Radiation* decision, many research protocols and informed consent processes change over the life of a study. This creates even more individualized issues that predominate over common issues. Similar problems occur in product liability class actions where a product or its warnings have changed over time. Such factors further reduce the number of factual issues that are common and typical to the class.

Proving medical causation is another factor likely to impede class action certification for human research lawsuits. Many participants have life-threatening illnesses in advanced stages and are receiving experimental treatment as their last treatment alternative. Whether a participant's death or injury was due to the experimental treatment or instead to the natural evolution of his preexisting illness is likely to be a disputed issue that must be resolved on an individualized basis.

Because of these and other issues, most courts are likely to deny certification of a class action brought by human research participants. Although the courts in three of the four cases discussed above did grant certification, those cases involved claims that the informed consent process was so fundamentally flawed that the participants essentially did not know they were being researched. In such circumstances, courts seemed more willing to conclude that common issues concerning the nature of the defendants' alleged misconduct predominated over individualized issues such as causation or reliance.

At first blush, it would appear that many of the recent cases asserting claims for dignitary harm may be more likely to be certified as class actions, as was *Diaz*. The *Diaz* court, however, admitted that the theory of dignitary harm was novel and untested, and since that time federal district courts in Oklahoma and Washington have rejected it as a viable cause of action.[80] In *Wright*, the plaintiffs did not even seek to certify their cause of action for dignitary harms as part of their proposed class.[81] As these cases suggest, the future of dignitary harm claims in general and as a basis to certify a class action is questionable at best.

The recent passage of the Class Action Fairness Act of 2005 (CAFA)[82] is likely to influence where future class actions involving human research subjects are filed and, in turn, may affect how future class certifications are decided. One of CAFA's purposes is to deter forum shopping, i.e., the filing of class actions in plaintiff friendly state courts with no substantial interest in the litigants or the claims, by granting federal courts broader jurisdiction over putative class actions. Among other things, CAFA expanded the definition of diversity jurisdiction by abolishing the requirement of complete diversity of citizenship and altering the amount in controversy requirement for purposes of class actions. As of February 2005, a class action may be brought in or removed to federal court as long as one plaintiff and one defendant are residents of different states. In addition, CAFA changed the amount in controversy requirement for class actions. Rather than requiring each class representative's claim to exceed $75,000, a class action may now be brought in federal court if the aggregated claims of the purported class exceed $5 million.[83] As a result of CAFA, many future class actions asserted by injured research participants are likely to end up in the federal court system. Although it is still too early to tell, CAFA may divert plaintiffs from filing class actions in certain state courts that have been more inclined to grant class certification motions in these types of cases.

The rise in the number of lawsuits involving clinical research has the potential to significantly impact medical and scientific research. Many commentators point out that litigation against researchers, insti-

tutions, IRB members, and sponsors is likely to discourage physicians from entering the research field, institutions from hosting valuable research, individuals from serving on IRB and other committees that evaluate research, and companies from developing new medical products and treatments. Some argue that it will cause IRB evaluation of research to become more conservative and legalistic.[84] An increase in the number of class actions lawsuits concerning clinical research could make these concerns even more daunting. Class action lawsuits give plaintiffs and their attorneys a greater ability to increase litigation and costs by rounding up persons who feel no reason to bring a lawsuit, threaten defendants with exorbitant claims of compensatory and punitive damages, and pressure them into settling lawsuits that lack merit. In the clinical research field, where most defendants are physicians and academic and medical institutions that are not regularly exposed to the nuances of litigation, these risks are even greater.[85]

Other commentators, including plaintiffs attorneys, however, feel that there is a useful role for litigation in the clinical research area. They argue that litigation is a good tool for deterring institutions and researchers from conducting—and IRBs from approving—overly risky, nontherapeutic research. Their position is that, until the regulatory oversight system is improved, litigation is an effective method of implementing changes in the way human research is conducted.[86]

Conclusion

Given the rise of litigation and class actions involving clinical research, those involved in conducting, hosting, approving, and sponsoring human research should keep abreast of the ongoing developments in this area of the law. In light of recent criticism and increased litigation, Congress may be prompted to enact comprehensive legislation setting uniform standards governing human research and creating one federal agency responsible for promulgating and enforcing regulations to protect study participants. Such changes are likely to be more effective than litigation at addressing the issues raised by human research participants. ■

Notes

1. Department of Energy, Advisory Comm. on Human Radiation Experiments, Final Report pt. I, ch. 1 (1995) [hereinafter Final Report], www.eh.doe.gov/ohre/roadmap/achre/index.html.

2. The Nuremberg Code, http://ohsr.od.nih.gov/guidelines/nuremberg.html; the Helsinki Declaration, http://ohsr.od.nih.gov/guidelines/helsinki.html.

3. Final Report, *supra* note 1, at pt. I, ch. 2. See also the texts of the Nuremberg Code and the Helsinki Declaration themselves.

4. Pub. L. No. 93-348, 88 Stat. 348 (1974).

5. National Comm'n for the Protection of Human Subjects of Biomedical and Behavioral Research, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, summary section (1979), http://ohsr.od.nih.gov/guidelines/belmont.html.

6. *Id*.

7. *Id. See also* Roger L. Jansson, *Researcher Liability for Negligence in Human Subject Research: Informed Consent and Researcher Malpractice Actions*, 78 Wash. L. Rev. 229, 233 (2003).

8. Final Report, *supra* note 1, at pt. I, ch. 3.

9. Roger L. Jansson, *supra* note 7, at 236.

10. Final Report, *supra* note 1, at pt. III, ch. 14.

11. *See* 45 C.F.R. § 46.103(b)(1); Roger L. Jansson, *supra* note 7, at 234. Before providing funding to an institution to conduct research, the DHHS requires that the institution provide an FWA that it will comply with common rule regulations. Part of the FWA requires institutions to attest that they will apply the common rule to all research it hosts, even research that is privately funded.

12. Final Report, *supra* note 1, at pt. III, ch. 14.

13. 45 C.F.R. § 46.107; 21 C.F.R. § 56.107 (2003).

14. 45 C.F.R. § 46.108; 21 C.F.R. § 56.108 (2003).

15. 45 C.F.R. § 46.111; 21 C.F.R. § 56.111 (2003).

16. 45 C.F.R. § 46.109; 21 C.F.R. § 56.109 (2003).

17. 45 C.F.R. § 46.103 (2003).

18. 45 C.F.R. § 46.115; 21 C.F.R. § 56.115 (2003).

19. 45 C.F.R. § 46.116; 21 C.F.R. § 50.25 (2003).

20. Mark Barnes & Patrik S. Florencio, *Investigator, IRB and Institutional Financial Conflicts of Interest in Human-Subjects Research: Past, Present and Future*, 32 Seton Hall L. Rev. 525, 527–28 (2002); Claire Hughes, *Drug Trial Under Scrutiny*, Albany Times Union, Mar. 30, 2003, at A1.

21. Barnes & Florencio, *supra* note 20, at 527–28.

22. 42 C.F.R. § 50.604 (2003).

23. 42 C.F.R. § 50.603 (2003).

24. Barnes & Florencio, *supra* note 20, at 537.

25. 21 C.F.R. § 54.4 (2003). *See also* Barnes & Florencio, *supra* note 20, at 537–38.

26. Barnes & Florencio, *supra* note 20, at 547.

27. Press Release, Food and Drug Administration, FDA Announces New Initiative to Modernize the Regulation

of Clinical Trials and Bioresearch Monitoring (June 26, 2006), www.fda.gov/bbs/topics/NEWS/2006/NEW01396.html.

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30. Jacob M. Appel, *Research Guidelines: Changes Urged*, 29 J.L. MED. & ETHICS 103, 104 (2001).

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