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Clinical Trials: 2018 Litigation And Guidance Roundup

By **Sheryl Bjork and William Childs** (January 3, 2019, 3:27 PM EST)

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Performing trials to evaluate the safety and efficacy of medicines and devices for a particular indication and patient population requires the navigation of complex medical, scientific, regulatory and ethical principles — and such trials, of course, often continue after approval as well, supporting additional indications and evaluating ongoing safety questions.

And so it is no surprise that issues relating to clinical trials feature prominently in many products liability lawsuits, as plaintiffs' attorneys try to show that corners were cut and something was missed — or intentionally avoided — in the study process, and as defense attorneys demonstrate the extensive work performed to learn about the medicine or device. The clinical trials themselves can become the direct subject of litigation as well, if a subject in a study believes an injury resulted from the trial.

2018 brought us litigation of both sorts, in addition to new proposed guidance from the U.S. Food and Drug Administration about how clinical trials ought to be performed — guidance that will, if adopted, be an important part of the regulatory story in litigation in the future.

Litigation About Clinical Trials

In 2018, courts considering product liability and professional malpractice claims looked at several issues relating to clinical trials: What is the scope of a trial sponsor's duty? What level of evidence is required to prove that participation in a clinical study caused a subject's injuries? What are the boundaries of a "lack of informed consent" claim — does such a claim even exist, or is it subsumed within another cause of action? Is an actual injury required to successfully assert that the patient did not give "informed" consent?

The Eleventh Circuit considered some of these issues in Looney v. Moore,[1] a case involving a national clinical research trial to study the effects of oxygen saturation levels in infants with extremely low birth weights. Parents of infants who participated in the study (and who alleged consequent neurological issues and retinopathy) sued the doctor who designed and ran the study, the institutional research board physicians who approved the study and the company that manufactured the medical equipment used. The plaintiffs (three children in the study) brought claims ranging from breach of fiduciary duty

and products liability to the amorphous “lack of informed consent” claim.

The courts’ analyses are illuminating. The trial court granted summary judgment in favor of the defendants.[2] On appeal, the Eleventh Circuit affirmed, determining that the plaintiffs had failed to prove, as required under Alabama law, that their injuries were “probably” caused by participation in the study, as opposed to a consequence of their premature birth. As a practical matter, this — reflecting the typical preponderance of evidence required in negligence cases — may be a high hurdle for clinical trial patients, given the challenge of distinguishing injuries from the clinical trial from those that would ensue from the underlying condition.

The Looney court also looked at the plaintiffs’ purported “informed consent” claim. The court refused to identify an “informed consent” claim on its own merits without attaching it to some other cause of action, such as medical malpractice or straight negligence. Ultimately, the court tied this claim to Alabama’s medical malpractice statute and common law negligence law to determine that, as in all tort claims, an “actual injury” is required to make a claim based on the patient’s lack of informed consent.

So even if plaintiffs’ “consent was not intelligently given, as a result of the incomplete information offered to them,” if they cannot show an “actual injury” caused by the study, then, under the Eleventh Circuit’s interpretation of Alabama law, they do not have a claim. Put another way, a breach of duty “in the air” does not by itself result in liability. That breach must cause harm. Because the absence of a causal link to any injury was lacking, the court had no reason to evaluate the question of whether a product manufacturer or an institutional research board can be liable for lack of informed consent.

The California Court of Appeals addressed the issues of duty and causation in the context of a product liability action against a clinical trial sponsor. In the unpublished decision Liu v. Janssen,[3] the court looked at issues of causation and duty of a clinical trial sponsor. In this case, the court overturned a $5.6 million jury verdict in favor of a parent whose child died after taking one dose of an antipsychotic drug being studied. Like the court in Looney, the Liu court determined there was insufficient evidence, even under the looser “substantial factor” test, to demonstrate that the trial treatment had a causal role in the patient’s death. According to the court, “a force which plays only an ‘infinitesimal’ or ‘theoretical’ part in bringing about injury, damage, or loss is not a substantial factor.”[4]

More interesting, however, was the court’s assessment of the study sponsor’s duty to trial participants. The factual scenario was somewhat unusual, in that plaintiffs apparently argued both that the study drug caused the child’s death and, alternatively, that even if it did not, the defendant should have intervened to refer the child to a specialist to address his preexisting heart disease. The court determined that while a manufacturer/sponsor of a clinical trial undertakes a general duty not to harm study participants as part of the clinical trial protocols, it does not undertake a duty to diagnose or treat a patient’s preexisting, life-threatening disease or to intervene in the medical care and decisions precipitated by a patient’s abnormal test results. That duty rests with the study physicians who bear the ultimate responsibility for the safety and health of participants in the trial.

Finally, a nonprofit and individuals involved in clinical trials sued the FDA in Center for Responsible Science v. FDA,[5] seeking to increase disclosures to subjects in studies. This case began in 2014 with a citizens’ petition. FDA responded that “extensive review” of the petition was required. Three years later, FDA responded with a six-page denial of the petition, which the Center for Responsible Science viewed as inadequate. The petitioners filed a lawsuit against FDA challenging the denial in April 2017. In April 2018, the United States District Court for the District of Columbia granted the FDA’s motion to dismiss, finding that the CRS lacked standing to bring the suit.[6]

In May 2018, the CRS filed an amended complaint and, once again, the FDA in August 2018 moved to dismiss on the same grounds. Yet again, and in a final blow to the CRS, on Oct. 22, 2018, the court determined that CRS fell short of establishing standing for the lawsuit to continue.[7] The CRS argued it had standing because it had diverted its resources "to picking up the slack left from the FDA's desertion of its duties."[8] Without getting into the machinations the CRS underwent to demonstrate some sort of organizational harm, the court was not convinced. Additional efforts to force greater oversight of clinical trials may well be in the offing — and, as discussed below, the FDA itself does seem to be trying to increase transparency in clinical trials.[9]

FDA Activity

In May 2018, the FDA and the DHHS issued a guidance for institutional research boards, with a "written procedures checklist" for IRBs.[10] The purpose of the guidance is to assist IRB staff responsible for preparing and maintaining written procedures. Among other things, the 55-item checklist includes items such as considering additional elements for informed consent, reviewing qualifications of investigators and staff, and considering whether the study involves subjects who are likely to be vulnerable to coercion or undue influence and what additional safeguards are in place to protect them.

In January 2018, FDA director Scott Gottlieb announced a pilot program to make more data available to the public for new drug trials. Currently, when a drug is approved, the FDA releases, via the Drugs@FDA website, certain information the agency used when reviewing the new drug application, or NDA. This includes summaries written by medical reviewers that capture their assessment of the data, the proposed labeling or other requirements, and other important, relevant data supporting safe and effective use.

The pilot program will include up to nine recently submitted NDAs. For these applications, if approved, the Center for Drug Evaluation and Research will release portions of the clinical study reports from the sponsor's NDA along with the action package following approval. The FDA will gather feedback about how useful posting portions of clinical study reports in this format might be for the drug research and development community, medical researchers and the public.[11]

Finally, in November, the FDA launched the MyStudies app to gather data for clinical trials and other research directly from patients. Patients can use the app to directly submit data to researchers, potentially enhancing the collection of "real world" data and evidence.

Contract Research Organizations

Litigation in 2019 will continue to mount, particularly relating to the use in clinical trials of contract research organizations. CROs have, of course, been used for years by companies big and small, but there is some indication that the scope of their work may be continuing to expand to include tasks previously done by the sponsors, including decisions about interim analyses and study decisions.

Companies need to be vigilant in drafting clinical trial agreements to ensure appropriate oversight and collaboration, as it is easy to picture plaintiffs attorneys criticizing the delegation of go/no-go decisions to outside companies — companies that may have a financial interest in continuing to pursue studies. While CROs can be tremendously useful, their use — as with everything else in the development process — should be considered with an eye not just to a thorough and careful analysis of the benefits and risks of medicines and devices, but also to how their use could be (mis)interpreted in future litigation.

Conclusion

Everyone in the drug and device development process is already cognizant of the complex and important issues clinical trials face — the pressing need for treatments of countless conditions, and the just-as-pressing need to properly measure the efficacy and risks of those treatments, both before and after approval. As they do so, in addition to the primary goals, they must be aware of the litigation implications, whether directly in relation to the clinical trials, or in products liability litigation where the adequacy of those trials is challenged.

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[1] Looney v. Moore, 886 F.3d 1058 (11th Cir. 2018).

[2] Looney v. Moore, No. 2:13-cv-00733 KOB, 2015 WL 4773747 (N.D. Ala.).

[3] Liu v. Janssen Research & Development LLC, Nos. B269318, B270332 (Cal. Ct. App. 2d Dist., filed Jan. 3, 2018).

[4] Id. (citing Bockrath v. Aldrich Chem. Co. Inc., 21 Cal. 4th 71, 79 (1999).

[5] Center for Responsible Science v. Gottlieb, 311 F. Supp. 3d 5 (D.D.C. 2018).

[6] Center for Responsible Science v. Gottlieb, 311 F. Supp. 3d 5 (D.D.C. 2018).

[7] Center for Responsible Science v. Gottlieb, No. 17-2198 JEB (D.D.C. Oct. 22, 2018).

[8] Id.

[9] https://www.clinicalleader.com/doc/crs-files-lawsuit-against-fda-0001.

[10] https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm512761.pdf.

[11] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592566.htm.