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No Right to an Experiment

The D.C. Circuit properly upheld the FDA's regime of drug approval.

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When the Food and Drug Administration is in the news on an issue concerning drug safety, it is usually because someone is asking whether the agency is doing enough to protect the public from unsafe drug products that have already been approved.

In a recent decision, however, an *en banc* panel of the U.S. Court of Appeals for the D.C. Circuit addressed the other side of the coin: whether, in the case of drugs for terminally ill patients, the FDA goes too far in keeping drugs off the market until they are proved safe and effective.

In that case, *Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach*, the Abigail Alliance, a group representing terminally ill patients, claimed for its members a constitutional right to potentially life-saving experimental drugs that had not yet been approved as safe or effective. The case presented the federal appeals court with a challenging case brought by very sympathetic plaintiffs.

On Aug. 7, however, the *en banc* court, by a vote of 10-2, ruled against the Abigail Alliance and in favor of the FDA, in our view correctly upholding the statutory regime that Congress had enacted.

Interestingly, this case has divided the patient community. The Abigail Alliance and its supporters assert that patients with life-threatening illnesses have a constitutional right to decide whether to risk treatments with drugs of uncertain safety and effectiveness. The alliance was formed by a father whose daughter, Abigail, died from cancer after a long, unsuccessful battle to receive treatment with experimental drugs that were ultimately approved. The emotional pull of its arguments in favor of increased access to potentially life-saving experimental drugs is powerful.

Other patient groups, some of whom we represented as amici curiae in the *en banc* proceedings, argue that the testing required by current law is necessary to give drug companies the incentive to conduct the expensive, clinical trials needed to identify drugs that are safe and effective. In these groups' view, allowing companies to market and profit from the sale of drugs not proved safe and effective would severely undermine the quality of U.S. health care because physicians and patients would be deprived of information necessary to determine which drugs work and which do not.

At the end of the day, however, the D.C. Circuit rejected the Abigail Alliance's campaign to alter the current FDA drug approval regime, thereby preserving the integrity of the clinical testing program that is critical to the FDA's mission to promote the public health. The Abigail Alliance has indicated that it intends to petition for a writ of certiorari from the Supreme Court.

Inevitable Tension

The recent case is the latest chapter in a decades-long debate over how to resolve what the FDA described in its correspondence with the Abigail Alliance as "the inevitable tension between early availability of products to patients . . . and the need to obtain sufficient data to provide a reasonable expectation of benefit and lack of excessive harm."

In the late 1970s, the issue of access to unapproved drugs surfaced in connection with cancer patients seeking the unapproved cancer drug Laetrile. Ultimately, the FDA prevailed in the Supreme Court, which in *United States v. Rutherford* (1979) held that the agency had properly denied access to Laetrile. Subsequently, a study conducted by the National Institutes of Health proved that, in fact, Laetrile is not effective.

In the early 1980s, patients pressured the FDA to speed up approvals of AIDS drugs and to increase access to unap-

proved, experimental versions of these drugs. The FDA responded by adopting many of their suggestions, and today several programs are available to terminally and seriously ill patients, allowing them access to unapproved therapies where no approved alternative exists.

These programs prohibit drug companies from profiting from the sale of unapproved drugs but permit companies to recover their costs associated with the manufacture, research, development, and handling of experimental drugs. Often, companies refuse to make experimental drugs available under the FDA's programs, preferring to wait until they can obtain final approval.

Drug Process

In this latest incarnation of the debate, the Abigail Alliance contended that, under the U.S. Constitution, denying terminally ill patients access to as-yet-unapproved drugs that have completed the first phase of testing violates substantive due process. Put another way, the Abigail Alliance argued that upon drugs' completion of limited Phase I testing, patients with life-threatening diseases have a constitutional right to those unapproved treatments.

To fully evaluate this argument, a brief review of the FDA drug approval process is appropriate.

The Federal Food, Drug, and Cosmetic Act prohibits the manufacture and sale of new drugs unless and until they are approved as safe and effective. Under the statute, a drug company must establish safety and effectiveness of a new product in a New Drug Application that contains "full reports of investigations which have been made to show whether or not [the] drug is safe for use and effective in use." Proof of safety and effectiveness is derived from data accumulated in human testing.

The clinical testing process is detailed and multilayered, lasting on average approximately seven years. Phase I testing involves the initial introduction of the new drug into humans, generally involves 20-80 subjects, and focuses principally on identifying a safe dose of the drug. Phase II testing typically involves several hundred subjects and focuses on both safety and effectiveness. Phase III testing generally involves up to several thousand human subjects, and the FDA uses its results to "evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physical labeling."

Phase I testing is a very small part of the overall clinical testing process, and it provides limited information as to the safety or effectiveness of the drug product under FDA review. The FDA frequently denies approval of new drug applications based on safety or effectiveness concerns identified after Phase I testing has been completed. Nevertheless, the Abigail Alliance argued that due process requires patients with life-threatening diseases be given access to largely untested post-Phase I drugs.

Specifically, the alliance sought from the FDA a regulation that would allow drug sponsors to market for-profit drugs that have passed through Phase I testing but have not yet been approved as safe and effective by the FDA. The FDA determined that the alliance's proposal "would upset the appropriate balance that [the FDA is] seeking to maintain, by giving almost total weight to the goal of early availability and giving little recognition to the importance of marketing drugs with reasonable knowledge for patients and physicians of their likely clinical benefit and their toxicity."

The Abigail Alliance filed suit on the constitutional issue, losing in the district court and then prevailing before a panel of the D.C. Circuit. The panel identified a fundamental right of access to post-Phase I drugs by analogizing to such common law concepts as self-defense, necessity, and interference with rescue, all of which, the panel held, supported an overarching right for people in peril to try to save their lives.

No Fundamental Right

On *en banc* review, the D.C. Circuit's majority opinion, written by Judge Thomas Griffith, first considered whether, under the two-pronged test set forth by the Supreme Court in *Washington v. Glucksberg* (1997), the substantive due process right claimed by the alliance was "fundamental" and therefore entitled to strict-scrutiny review.

The D.C. Circuit held that the claimed right failed the first *Glucksberg* criterion—that the right be "fundamentally rooted in this Nation's history and tradition"—and that there was therefore no need to consider the second criterion—whether the right was "implicit in the concept of ordered liberty."

The court pointed out that "our Nation has long expressed interest in drug regulation, calibrating its response in terms of the capabilities to determine the risks associated with both drug safety and efficacy." The court traced this history back to colonial times, noting the regulatory efforts of the colony of Virginia in 1736, through the 1962 amendments to the Federal Food, Drug, and Cosmetic Act requiring that drugs be reviewed by the FDA for effectiveness as well as safety.

The court added that increased government regulation of drugs over time was in large part because of advances in technology that allowed the government to identify previously unrecognized risks and advances in the science of clinical trials, not because of a deviation from the view that a consumer is better situated than the government to evaluate known risks presented by an untested drug. The *en banc* court also determined that traditional common law tort concepts such as self-defense were dissimilar to the right to access claimed by the alliance and therefore did not support the conclusion that the right was deeply rooted in American history.

Having concluded that the alliance's claimed right was not subject to strict scrutiny, the *en banc* court easily found that "the Government has a rational basis for ensuring that there is a scientifically and medically acceptable level of knowledge about the risks and benefits" of potentially toxic drugs. In rejecting the constitutional argument, however, the court also recognized that the balance between access

and testing was an appropriate subject for continued debate involving the public, the FDA, and the political branches of government.

Judge Judith Rogers, the author of the panel opinion that had upheld the Abigail Alliance's constitutional claim, dissented from the *en banc* majority opinion and was joined by Chief Judge Douglas Ginsburg.

Patients with life-threatening illnesses who seek greater access to alternative therapies have made an important contribution to the debate about the appropriate level of drug regulation. In our opinion, however, it is critical that expanded access not undermine the process that Congress mandated in the Federal Food, Drug, and Cosmetic Act to determine which drugs are safe and effective. Tilting the balance too far in favor of access could destroy the incentives in current law that require drug companies to establish that drugs are safe and effective before they may be marketed to patients and sold at a profit.

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