FDA Guidance Lowers Bar on Early Drug Testing

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Researchers now have a pathway for conducting early clinical testing of drugs in a small number of human subjects under new guidance from the Food and Drug Administration.

Officials at the FDA finalized guidance on exploratory investigational new drug (IND) studies that allows researchers to move forward with small human studies before beginning traditional phase I safety testing in humans. The guidance, published in January, makes recommendations on safety testing, manufacturing, and clinical approaches in these early studies.

The FDA also published draft guidance and a direct final rule last month that outlines new standards for the manufacture of drugs solely for use in phase I studies. The rule is aimed at making it easier for scientists to produce small quantities of drugs for small-scale, early-phase human testing.

"This is about saving lives and about building medicine's future," said Dr. Andrew von Eschenbach, acting FDA Commissioner of Food and Drugs.

Currently, fewer than 10% of IND applications for new molecular entities progress beyond the investigational stage, according to the FDA. These changes will remove some of the hurdles from very early drug development, Dr. von Eschenbach said during a media teleconference sponsored by the FDA.

But critics of the approach say it relaxes needed human subjects protections at a time when the safety of clinical trials is already being questioned.

In guidance on the exploratory IND, FDA officials outline their thinking that drug sponsors have not taken full advantage of the flexibility in the existing regulations and often provide more supporting information than is required for an exploratory IND.

Exploratory IND studies involve administering either a subpharmacologic dose of a product or doses that are expected to produce a pharmacologic but not a toxic effect, so the risk to human subjects is considered lower than in a traditional phase I study, FDA said in its guidance documents.

Because exploratory IND studies pose fewer risks, FDA said, they can be initiated in humans with less, or different, preclinical support than what is required for traditional IND studies.

Previously, one of the major obstacles in the development of new drugs was that the requirements for beginning early experimental studies were the same as those for large pharmaceutical companies who are making drugs for thousands of patients, Dr. Steven Rosenberg, chief of surgery at the National Cancer Institute, said during the teleconference.

"We've been at the mercy of large biotech and pharmaceutical companies who have the resources to fulfill the very stringent regulations that exist for taking these new products to very large numbers of patients," he said.

The changes made by the FDA will make it possible for scientists to take new ideas to small numbers of patients with desperate diseases and test those agents in ways that weren't possible before, he said. Dr. Rosenberg said he expects to see a lot of ideas tested now that might not otherwise have been taken to patients under the old framework.

But Dr. Sidney Wolfe, director of Public Citizen's Health Research Group, said he remains concerned that the usual protection for human subjects has been "watered down." Under the new process outlined by the FDA, a safety problem that might have been detected through more extensive animal studies now may be missed, he said.

And he is doubtful of the benefits. Dr. Wolfe said the types of studies described in the exploratory IND are already being done but with the previous protections in place for human subjects.

Sen. Charles Grassley (R-Iowa), chairman of the Senate Committee on Finance, which has been conducting oversight of the FDA's consumer protections, also expressed safety concerns.

"Of course people want to get safer, better drugs faster, but there have to be sufficient checks and balances in the drug approval process," Sen. Grassley said in a statement. "At a time when new questions are being raised about whether participants in clinical trials are protected and treated ethically, the FDA is loosening the reins on drug companies." ■