FDA and the Drug Development Process:
How the Agency Ensures That Drugs are Safe and Effective

To treat patients in 1534 in a plague-stricken German town, Paracelsus, the famous Swiss physician and chemist, made pills on the spot from locally baked bread. Today, the process of bringing a drug to a patient's bedside takes an average of 8.5 years, costs about $500 million, and includes a rigorous review by the Food and Drug Administration. Unlike Paracelsus' bread pills, however, FDA-approved drugs meet the highest scientific standards and are demonstrated to be safe and effective.

Most modern drug development starts in laboratories, where scientists probe the effects of chemical compounds on enzymes, cell cultures or other substances involved in the disease whose treatment they seek. The potentially effective chemicals are then tested in two or more species of animals to determine whether they can be safely used in humans. No more than 5 in 5,000 tested compounds pass these preclinical trials and are proposed for clinical studies.

If the FDA finds the approach promising and an institutional review board of scientists, ethicists, and health-care specialists approves the sponsor's study protocol, the drug enters a progression of tests in humans. Each new trial phase is predicated on a successful outcome of the previous one:

- **Phase I studies** test the product for its adverse effects on a small number of healthy volunteers.
- **Phase II studies** probe the drug's effectiveness in patients who have the disease or condition the product is intended to treat.
- **Phase III studies** seek to determine the drug's safety, effectiveness and dosage. In these trials, hundreds or thousands of patients are randomly assigned to be treated either with the tested drug or a control substance, most frequently a placebo.
- The results of Phase III trials are submitted to the FDA for review by a team of chemists, physicians, epidemiologists and other specialists. This group's crucial task, which is frequently shared with an advisory panel of outside experts, is to judge whether the trials have demonstrated that the product's health benefits outweigh its risks. Only products that pass this test may be approved for marketing.

For more information, visit the FDA's Web site at *www.fda.gov/cder/handbook/*.

Helping Patients, Fast

The FDA frequently uses timesaving processes for speeding important new drugs to patients who need them:

- **Accelerated approval** may be granted to priority drugs that show promise in the treatment of serious and life-threatening diseases for which there is no adequate therapy. Priority drugs are sometimes judged for their effect on a surrogate marker that may predict clinical benefit to patients—such as the shrinking of cancer tumors—and their approval is followed by Phase IV trials to test their long-term effectiveness.
- **Treatment Investigational New Drug (IND) designations** enable patients not enrolled in the clinical trials to use promising life-saving drugs while they are still in the testing stage. For example, when the first tests of the antiviral drug AZT in 1985 showed encouraging results in 330 AIDS patients, the FDA authorized a treatment IND for more than 4,000 people with AIDS before AZT was approved for marketing.

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