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The Drug Development and Approval Process

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The U.S. system of new drug approvals is perhaps the most rigorous in the world. On average, it costs a company $500 million to get one new medicine from the laboratory to the pharmacist's shelf, according to a January 1996 Boston Consulting Group study.

It takes 15 years on average for an experimental drug to travel from lab to medicine chest, according to the Tufts Center for the Study of Drug Development, Tufts University. Only five in 5,000 compounds that enter preclinical testing make it to human testing. And only one of those five is approved.

Once a new compound has been identified in the laboratory, medicines are developed as follows:

Preclinical testing. A pharmaceutical company conducts laboratory and animal studies to show biological activity of the compound against the targeted disease, and the compound is evaluated for safety.

Investigational New Drug Application (IND). After completing preclinical testing, the company files an IND with FDA to begin to test the drug in people. The IND becomes effective if FDA does not disapprove it within 30 days. The IND shows results of previous experiments; how, where and by whom the new studies will be conducted; the chemical structure of the compound; how it is thought to work in the body; any toxic effects found in the animal studies; and how the compound is manufactured. In addition, the IND must be reviewed and approved by the Institutional Review Board where the studies will be conducted, and progress reports on clinical trials must be submitted at least annually to FDA.

Clinical Trials, Phase I. These tests involve about 20 to 80 normal, healthy volunteers. The tests study a drug's safety profile, including the safe dosage range. The studies also determine how a drug is absorbed, distributed, metabolized and excreted, and the duration of its action.

Clinical Trials, Phase II. In this phase, controlled studies of approximately 100 to 300 volunteer patients (people with the disease) assess the drug's effectiveness.

Clinical Trials, Phase III. This phase usually involves 1,000 to 3,000 patients in clinics and hospitals. Physicians monitor patients closely to determine efficacy and identify adverse reactions.

New Drug Application (NDA). Following the completion of all three phases of clinical trials, the company analyzes all of the data and files an NDA with FDA if the data successfully demonstrate safety and effectiveness. The NDA must contain all of the scientific information that the company has gathered. NDAs typically run 100,000 pages or more. By law, FDA is allowed six months to review an

NDA. The average NDA review time for new molecular entities approved in 1995 was 19.2 months.

Approval. Once FDA approves the NDA, the new medicine becomes available for physicians to prescribe. The company must continue to submit periodic reports to FDA, including any cases of adverse reactions and appropriate quality-control records. For some medicines, FDA requires additional studies (Phase IV) to evaluate long-term effects.

Discovering and developing safe and effective new medicines is a long, difficult and expensive process. The research-based pharmaceutical industry will invest $15.8 billion in research and development this year.

The Drug Development and Approval Process in the '90s

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	Early Research /Preclinical Testing	File IND at FDA	Clinical Trials			File NDA at FDA	FDA		Phase IV
			Phase I	Phase II	Phase III				
Years	6.5		1	2	3		2.5*	15 Total	
Test Population	Laboratory and animal studies		20 to 80 healthy volunteers	100 to 300 patient volunteers	1000 to 3000 patient volunteers				
Purpose	Assess Safety and biological activity		Determine safety and dosage	Evaluate effectiveness, look for side effects	Verify effectiveness, monitor adverse reactions from long-term use		Review processs/ approval		Additional post-marketing testing required by FDA
Success Rate	5,000 compounds evaluated		5 enter trials				1 approved		

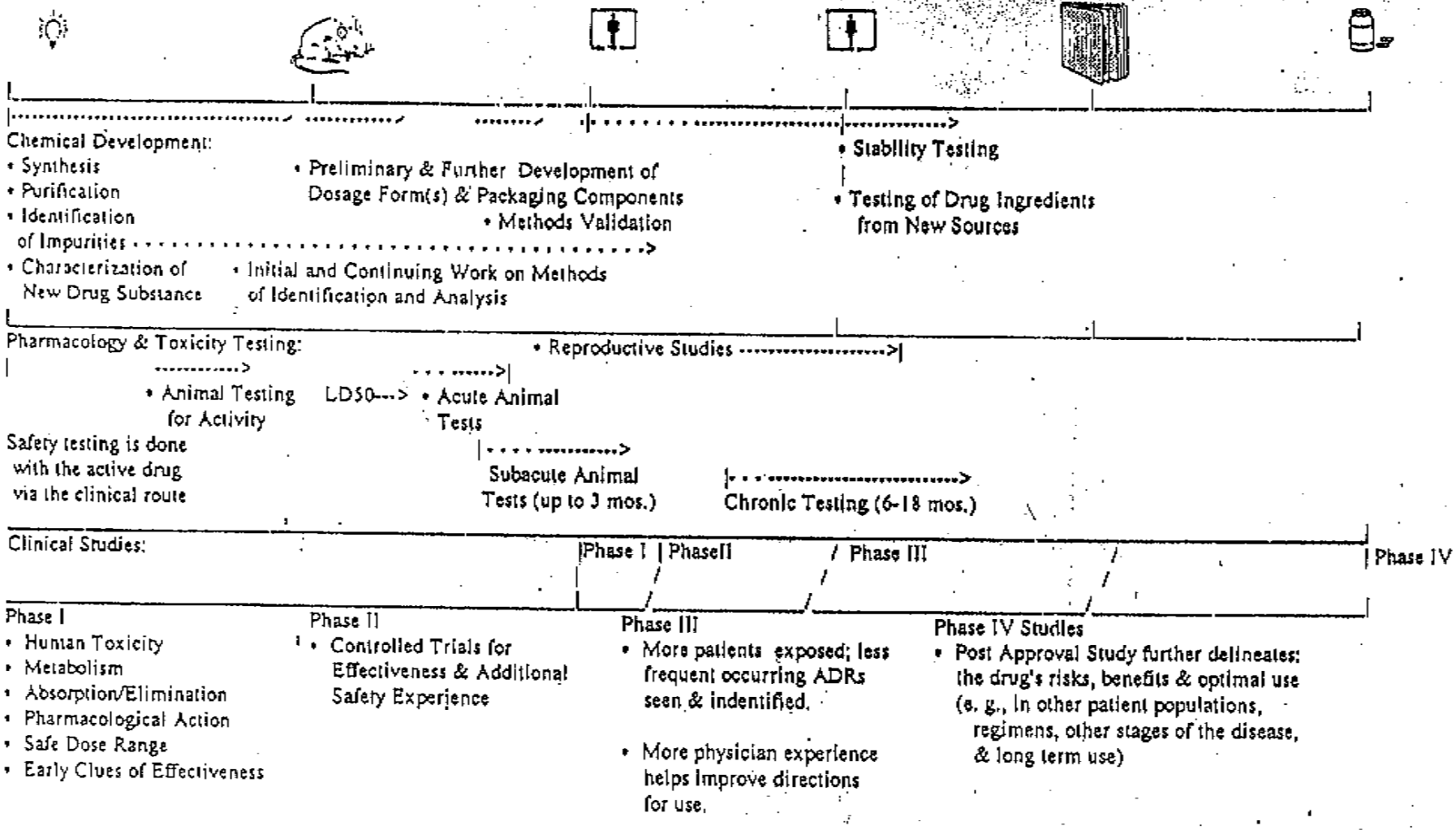

FIGURE 1. Drug Development Time Line.