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Module 2 – Understanding the Research Process and R&D Decision Making

Drug R&D Part One: Understanding the Process for New Medicines

All new therapies that work through a chemical action in the body are developed through a process commonly called the drug development pathway. These types of therapies include small molecule drugs and biologics.

Small molecule drugs are medicines made through chemical synthesis. Common examples include antibiotics, steroids, and pain medicines.

Biologics are medicines derived from natural sources. Examples include proteins like insulin, antibody therapies, cell and gene replacement therapies, and vaccines.

The simplest way to understand the drug development pathway is to look at it as a series of experiments that answer a specific set of questions about how a treatment works, whether it is safe and effective, and how to use it. These experiments must be conducted in a specific order, and the results must be reviewed by regulatory officials at specific checkpoints. The steps are organized this way to minimize the risks of giving people a medicine while we are still learning about it.

The earliest steps in drug R&D are called discovery and preclinical research. This research is conducted in cells and animals.

In discovery research, the goal is to make or find a set of molecules that have chemical and biological properties that could treat a health condition. These molecules are called “drug candidates.”

To understand what properties a drug candidate needs to have to treat an injury or illness, discovery scientists rely on information from basic research about how our bodies work and what happens when we are sick or injured. We will talk more about basic research later in this module.

Discovery researchers may test thousands of molecules to find a handful of candidates that have the right chemical and biological properties. These candidates enter preclinical development.

Preclinical experiments show how the candidates work in cell and animal models that simulate a human health condition. Some of these experiments help predict whether the candidates will

provide a treatment benefit in people, and some test for toxicity to see whether the candidates are safe enough to be tested in people.

When this work is done, it is submitted to regulators in an application requesting permission to test the drug candidate in clinical trials. This review is the first of many steps during drug R&D that assure people who volunteer as participants in clinical trials are protected from harm.

If the application is cleared, then clinical development can begin. Clinical development is the first time a drug candidate is given to people.

Most new medicines go through three phases of clinical development before they are approved.

The first step is usually Phase 1 testing. Phase 1 trials test a drug candidate's safety and monitor what happens to it in the body – where it goes, how it gets there, how is it broken down (or "metabolized"), and how it leaves the body. This information helps clinical researchers determine what doses of the drug should be studied in the next phase.

Phase 2 trials are usually the first time a drug candidate is evaluated for "efficacy," which means how well it works to treat a health condition. Phase 2 trials may also test different ways of administering the drug candidate, and help choose the doses that will be used in Phase 3 trials. A drug candidate is usually tested in several different Phase 2 trials.

Phase 3 trials confirm that the drug is effective and safe, and determine the best ways to use it. In most cases, two successful Phase 3 trials are required before a drug candidate can be approved.

Throughout clinical development there are multiple layers of protection for the people who participate in trials.

First, the numbers of people who receive an experimental drug start small when we know the least about it, and increase as we learn more.

In addition, each trial must be approved by an Institutional Review Board, or IRB, before it can start. The IRB reviews the study design to ensure it is medically, ethically, and legally acceptable. The IRB also reviews all patient and physician materials, including informed consent forms.

Under informed consent, every potential volunteer must be given all the facts about the trial, and must formally agree to participate. A volunteer can withdraw consent and leave a trial at any time for any reason.

Each trial is also monitored for adverse events to decide whether it is safe to continue. Large, complex trials, especially Phase 3 studies and other trials that present risks to participants, are monitored by an independent scientific committee called a Data Safety Monitoring Board, or DSMB.

When clinical testing is finished, the drug company submits an application to regulators to ask for marketing approval. The application contains all the data from preclinical and clinical studies, plus information on the manufacturing process and quality controls. Using these data, regulators must decide whether or not the drug is safe and effective enough for a specific use, in specific people with a specific health condition.