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

Drug R&D Part Two: Who decides?

The step-by-step process of drug R&D is fairly straightforward. But how that process gets done is very complex. For the people who do the work, R&D is best understood as a series of decisions and trade-offs that have to be made based on imperfect information, by different people who have different goals and responsibilities.

The two main decision-makers in commercial drug development are drug sponsors, and regulators.

Most sponsors of approved drugs are pharmaceutical or biotech companies. Sometimes they develop new treatments all the way from discovery to regulatory approval, but often they acquire a drug candidate from a smaller company, an academic institution, or independent researchers at an early stage of development. We will talk more about how academic and independent researchers who do drug discovery make decisions later in this module.

Pharmaceutical and biotech companies' goals and responsibilities are to develop treatments that help people with injuries or illnesses, and to make money doing it.

They have many decisions to make during R&D, including:

- Which disease or condition to work on?
- What molecules to test?
- What studies to conduct?
- Which people to treat?
- What outcomes to measure and what data to collect? And, at each stage of development,
- Whether to stop or keep going?

The other major decision-makers – regulators -- have a completely different set of goals and responsibilities, and have different decisions to make during drug R&D. Different countries have different regulatory bodies. For instance, the Food and Drug Administration, or FDA, regulates drug approvals in the United States, while Health Canada regulates this process in Canada, and the European Medicines Agency, or EMA, regulates drug approvals in the European Union.

Regulators have two main responsibilities: to protect people from being harmed, and to promote public health by approving safe and effective drugs.

Regulators decide:

- What evidence is needed to allow clinical testing?
- What studies and outcomes are required to approve a drug?
- What balance of benefits and risks justifies drug approval? And
- What drug sponsors will be allowed to say about the drug's uses, benefits, and risks after it is approved.

What this means is that even though drug sponsors technically can independently decide what studies to do and what outcomes to measure, they would be foolish to make choices that regulators will disagree with.

So how *do* drug sponsors make decisions?

In addition to considering what regulators will require for drug approval, sponsors consider many different factors that affect their ability to meet their goals: to help people who are sick or injured, and to make money.

Drug sponsors consider:

- How big the medical need is,
- How much scientific knowledge there is about the condition,
- Whether they have the right technical and scientific abilities to develop the drug,
- The financial resources needed to develop the drug, and
- Whether there is enough intellectual property protection, such as patents, to protect their investment.

The stakes are extremely high, because developing a single drug takes a long time and costs a lot of money. On average, the entire process from discovery to approval takes 10 years. The average out-of-pocket R&D costs from discovery to approval for just one drug is $1.4 billion.

But most drugs do not make it. Nine out of every ten drugs that enter Phase 1 testing fail or are discontinued, and usually after Phase 2 testing, when a lot of time and money have already been spent.

Now, let's look at how regulators approach decision-making, which is very different from how drug sponsors make decisions.

Regulators focus on weighing benefits against risks. Benefits generally include improvements in how a person receiving a treatment feels, functions, or survives. Risks include side effects from treatments, but also the risk that health will worsen if no treatment or an ineffective treatment is given.

At first glance, it may seem that risk-benefit decision making is more straightforward than the numerous factors that drug sponsors take into consideration. But risk-benefit is a judgement call.

No matter how many clinical trials have been done, and how much data are collected, it is impossible to know how a new drug will affect all the different types of people who could receive it after it is approved. So regulators have to weigh both the risks and benefits they know about from the preclinical and clinical data, and the ones that might only turn up after the drug is approved and given to many more people.

There is no better judge of risk-benefit than the people who live with the health condition that a new drug is supposed to treat. That is why the perspective of research advocates living with health conditions – like SCI – is so important during drug R&D.