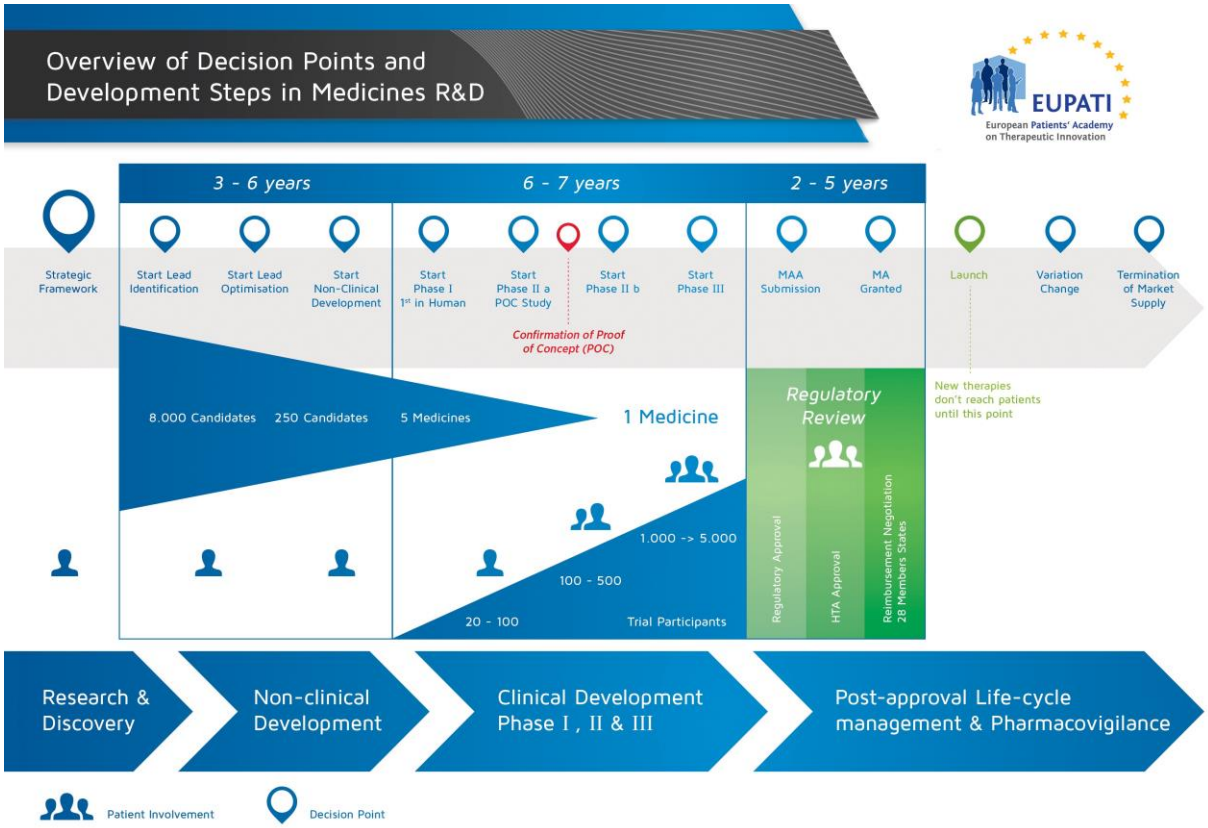
Fact Sheet: Making a medicine – Medicine discovery

It takes over 12 years and on average costs over €1 billion to do all the research and development necessary before a new medicine is available for patients to use.

Medicines development is a high-risk venture. The majority of substances (around 98%) being developed do not make it to the market as new medicines. This is mostly because when you look at the benefits and risks (negative side effects) found during development, they do not compare well with medicines that are already available to patients.



The medicines development process

The steps involved in medicine discovery are described below.

STEP 1: Pre-discovery

Scientists in academia (universities) and in the industry (pharmaceutical companies) work to understand the disease.

STEP 2: Target selection and unmet needs

Diseases occur when the normal body processes are altered or not functioning properly. When developing a medicine, it is important to understand in detail (at the level of the cells) what has gone wrong. This allows the abnormal process to be 'targeted' and corrected. The 'target' may be a molecule that has been produced in excess, interfering with normal body

function, a molecule that is not being produced in normal amount, or a molecule that has an abnormal structure. For example, in cancer there can be too much of a chemical messenger, signalling the cells to grow abnormally; in diabetes, there is a lack of insulin production or cells don't respond to it normally.

Before development on a new treatment begins, it must also be determined whether or not there is an unmet need. An 'unmet need' refers to a disease where either there is no suitable medicine available, or, if there is a medicine already available, some patients might be unable to take it due to unacceptable side effects. If there are identifiable cases in which a need for treatment is unmet, development of a new treatment will go ahead.

STEP 3: Lead generation

This step involves finding a molecule which will interact with the target. The molecule may come from a natural source (for instance, a plant), or it may have been made by chemists. Hundreds of thousands of molecules will be tested to find 'leads' – molecules that interact with the target. The process of testing for leads is called a screening process. Modern robotic technology allows for high throughput screening. This means that millions of molecules can be tested quickly. Once leads have been generated (or found), the process can move to the next step.

STEP 4: Lead optimisation

After the screening process has identified leads, modifications of these molecules are often required in order to improve their effect – often the leads that are found have only a weak effect on the target and would otherwise be unsuitable for further development.

In order to optimise these leads, chemists alter the lead molecule by adding or removing some of its elements, creating a range of slightly different molecules. The molecule of a previously existing medicine may also be modified or improved and its effect changed in this manner. Computer technology can also help in designing these modified molecules.

The modified molecules are then tested to determine which structure has the best efficacy and safety (whether it is tolerated by the body). These studies help to gain understanding of the pharmacology of the molecule (the way the molecule works on the body). The molecules with the best efficacy and safety can then proceed as a 'candidate drug'.

At around this time, the scientific and technical information about the candidate compound, such as its molecular structure and effects, is usually registered, or patented, in order to protect it as intellectual property.

STEP 5: Non-clinical safety testing

Medicines development is tightly controlled. The law imposes rules and regulations about what is done and how it is carried out. No candidate medicine can be tested in humans (in clinical studies) before its safety profile has been established in animal safety studies. This next stage in the development process, non-clinical safety testing, aims to establish whether it is safe to proceed with the candidate compound into clinical studies.

Before the non-clinical testing work can be done, larger amounts of the candidate drug need to be produced so that all the appropriate tests can be carried out. This manufacturing

process must follow strict guidelines and regulations known as Good Manufacturing Process (GMP).

Non-clinical safety testing involves testing in animals. These tests are is governed by the specific rules and regulations of Good Laboratory Practice (GLP). The studies not only show the safety profile in animals, but also provide important information on:

- Absorption (how the medicine enters the body)
- Distribution (how the medicine travels around the body)
- Metabolism (how the medicine is broken down by the body)
- Excretion (how the medicine leaves the body)

These four factors are abbreviated to ADME.

All of this information is used to decide whether the candidate drug can proceed into the first human (clinical) study, and if so, what dose should be used.