13. Drug Discovery and Development

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The long and costly path (DiMasi et al., 2016) that must be followed before a new medicine is approved by the relevant regulatory authority (e.g., the FDA in the United States of America and ANVISA in Brazil) is generally divided into two phases (Blass, 2015): the discovery phase (*Drug Discovery*), sometimes referred to as the Research phase, and the development phase (Drug Development)**.**

Considering the case of traditional drugs (small molecular entities), and not biopharmaceuticals, the **DISCOVERY** phase involves all the steps required to obtain a drug candidate ready to be submitted to clinical studies (see the definitions of hit, lead compound, and drug candidate). In the case of a target-based drug discovery strategy, the discovery phase begins with the identification of a molecular target for which several active substances (hits) will initially be sought, usually through a high-throughput screening (HTS) process. The drug discovery phase then proceeds with the identification of a few lead compounds which, after optimization, yield a drug candidate. It should be noted that the same outcome can be achieved using a phenotypic drug discovery strategy, which starts directly with the identification of active substances without any prior assumption regarding the molecular target(s) (Swinney and Anthony, 2011; Mullard, 2015). The drug discovery phase is also referred to as the "preclinical" phase and consists of *in vitro*, *ex vivo*, and *in vivo* studies, including pharmacology and toxicity studies in animals.

On the other hand, the **DEVELOPMENT** phase involves clinical studies (Phases 1, 2, and 3) as well as non-clinical studies in animals that are conducted simultaneously, including subchronic and chronic safety studies, complementary reproductive toxicology studies, and carcinogenicity studies (Andrade et al., 2016). Therefore, the initiation of clinical trials can be considered the dividing line between the two phases.

These definitions are consistent with guidelines published with support from the NIH (Hughes et al., 2012) and also with the perspective of PhRMA, an influential association representing the major innovative biopharmaceutical research companies in the United States of America.

On the other hand, some authors consider that the development phase begins with "preclinical development", which involves studies using an already optimized lead compound, such as detailed pharmacokinetic studies in animals, acute toxicity studies, as well as formulation studies and large-scale synthesis ("scale-up"). After authorization by the regulatory authority, the phase of clinical development begins, as described above.

References

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