

Backgrounder

Pharmaceutical Development – From Raw Material To Active Agent

Despite the tremendous progress of biomedical science, there are still tens of thousands of known diseases with no effective treatment. History has shown that it can take up to 12 to 15 years until a drug finally becomes available in pharmacies, at development costs of about 800 million Euros. Clearly, there is a need to improve the drug discovery process.

The data of many millions of active ingredients are already stored in international “substance libraries,” more new substances that are possible active ingredients are being found in plants or microorganisms, and research labs are working on the development of synthetic substances every day. To examine or “screen” all of substances for their effectiveness as a potential drug, new, highly parallel analytical techniques are needed. Chip-based methods that improve and accelerate the efficient finding of new drugs hold great promise in this area.

New biochips from Infineon can be used in several phases of pharmaceutical development: the Flow-Thru technology permits analysis of the effectiveness of substances within a few hours. Given the large number of substances to be tested, highly parallel analytical techniques such as the FTC can shorten the overall development cycle for a drug by about one or two years. One benefit of this is that treatment for patients can become available earlier. Furthermore, the advantage in time could mean a considerable increase in revenues for the pharmaceutical industry: A so-called blockbuster – i.e. a popular new drug – could generate average annual revenues of about 500 million Euros before the patents on the drug and its active ingredient expire. Within this period of time, the company must earn an amount that equals the development costs, which will also enable it to advance the research for other drugs.

After initial screening of thousands of substances, only a few out of several thousand possibilities will qualify as viable drug candidates. In cell cultures, on isolated organs

from animals, in a variety of biochemical experiments and by means of many other methods, scientists examine whether the substances have the expected healing effect.

Clinical Tests

Upon completion of these preliminary investigations, which takes three to five years, a candidate drug will enter the first phase of clinical testing. Initially, an ethics commission will decide on the necessity and usefulness of the experiments. The drug is then administered to healthy individuals. Phase One determines whether humans tolerate the active ingredient and how this agent is distributed, processed, consumed and excreted. In addition to the effectiveness for the human organism (pharmacodynamics), the duration of effectiveness (pharmacokinetics), side effects and toxicity as well as the possible forms of administration (galenics) are examined. After all, a variety of factors determine whether a drug is administered by injection, as a tablet or as an ointment.

Once Phase One is successfully completed, voluntary tests are conducted to find out how sick patients respond to the potential new drug. In addition to determining the compatibility with the patients, this focuses on the therapeutic effect of the drug. Such tests usually involve a high number of patients, up to 500 to 1,000, who take the drug under strict clinical supervision over a period of about four to six weeks. The findings about the effectiveness determine whether the drug will enter the third phase of clinical testing.

In this last phase before approval, the tests are extended to include several thousand patients in order to test the effectiveness on a broad base. The drug must not be harmful even if applied over an extended period. Side effects and interactions with other drugs are documented. The researchers also compare the effectiveness of the new drug to that of standard products that are already commercially available. If no standard product is available, the drug is tested against a product that does not contain an active agent, a placebo.

Approval

Competent authorities for the approval of drugs are the German Bundesinstitut für Arzneimittel und Medizinprodukte, the Paul Ehrlich Institute, the European approval agency (EMA) in London. Without their approval, a pharmaceutical company is not allowed to market a new drug. Once the approval has been granted, which is 12 years after the start of the project on the worldwide average, the new drug is available for

patients. In the years to follow, its compatibility will be monitored and its effectiveness will be further developed and optimized.

This backgrounder is based upon information from the following sources:

www.bpi.de: Bundesverband der Pharmazeutischen Industrie (BPI) e.V., Berlin: Presentation by Dr. Gudrun Tiedemann on the subject of "Pharmaceutical development: Biopharmaceutical drugs - Status and future" at the GBF - BioProfil – BioRegionN Symposium on December 4, 2002.

www.vfa.de: Verband forschender Arzneimittelhersteller, collection of background texts on the Web site.

www.krebs-kompass.de: A cancer information forum on the Internet, initiated by the non-profit Volker Karl Oehlrich-Gesellschaft e.V., Riedstadt. The Internet site is committed to observe the statutes that were defined by the Geneva Health on the Net Foundation (www.hon.ch) with respect to health information on the Internet.

www.gesundheitslexikon.de: This health almanac is managed by the editors of *Neue Apotheken Illustrierte/Gesundheit*, an independent trade magazine. It is published by GOVI-Verlag, Pharmazeutischer Verlag GmbH, the publishing house of the umbrella organization of German pharmacies "ABDA".

At www.krebs-kompass.de, the comparison with the placebo is placed at the end of phase II, while the VfA assigns this comparison to phase III. The author prefers to adopt the VfA view.

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