# Symposium on Licensing and the Use of Biotechnological Drugs Development
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**President of the Symposium**
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## ABSTRACTS

### The Situation of Biotechnological Drugs in Turkey

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The share of biotechnological and biosimilar drugs in the total drug market is increasing. In our country this percentage has reached 20% levels and by 2025, the total percentage of those drugs is expected to exceed 30% worldwide. In our country, 23 members are present in the Turkish Biotechnological Drugs Platform established with the leadership of İEİS, and more than half of the members have serious investments in this field. Among the projects about the biotechnological drugs, 34 mAbs are present which are expected to be completed in the next 5 years. Until now, 19 biosimilars have been registered. On the other hand, European Union acted very early and fast in the field of biosimilars. Since the approval of first biosimilar in 2006 in EU, 44 biosimilars have come out to the market. The market share of these products have exceeded 50%. With the widening of biosimilar usage, the number of patients that can reach the therapy with such drugs have increased, additionally positive contributions have been observed to health expenditure. In EU over 700 million patients have been reached. By this time, it has been shown that biosimilars are indistinguishable from the reference product in terms of efficacy and safety by various clinical trials.

### Development of Biotechnological Drugs

Hamdi Akan
Clinical Research Society

The problems in the development of conventional drugs, the limitations in the development of new drugs in the field of infections threatening public health and for the treatment of diseases like obesity and Alzheimer which have become a serious problem with the development and aging of the society and the failure of drug development efforts for the treatment of spreading diseases have constituted a serious problem. But in the same period, the quick distribution of the term targeted therapy has been widened in the fields of hematology, oncology and romatology and high investments have been done and a huge amount of new drugs appeared in those fields. The most important reasons for the development of this field are: (A)The shortening of the drug development period by the use of correct software, (B)The good results obtained by targeted therapies in vairous fields, (C) The adverse effects of targeted therapies arer less than conventional therapies, (D) In clinical trials performed by biological agents, clinical end points are replaced by biomarkers and the duration is very short, (E) The support and encouragement given by the health authorities for the development of biological agent and biosimilar products.
This field has diadvantages and advantages:
(A) The development of biological agent is costly. Therefore authorities support the development of biosimilars. For example, in USA, the decision of waiting for 6 months after a biosimilar is authorised has been cancelled by the supreme court. However, the most important point is there is a short time for the marketing of a successful biological agent and becoming profitable an it is a highly profitable field(http://klinikarastirmalar.org.tr/New/1232/bir-onkoloji-ilacının-gelistirilme-maliyeti). In the clinical trials done by biological agents, health authorities like FDA gives provisional approval at Phase I or Phase II and the drug can reach to the patients very fast but there very significant objections in this field. These provisional approvals are expected to be re-evaluated after Phase III but this is not done and some biological agents which are useless are on the market (Assessment of Overall Survival, Quality of Life, and Safety Benefits Associated With New Cancer Medicines, SV Sebastian et al. JAMA Oncol. 2017;3(3):382-390)
(B) The biological agents are sold in very high prices. The 8 of top 10 pharmaceuticals are biological agents (QuintilesIMS 2016 National Sales Perspective)
(C) The rate of failure during the development of biological agents is very high. Hematology is a lucky field in this subject, 26% of the drugs reaching phase I are registered, in oncology this rate is only 5% (2006-2015 Clinical Development Success Rates 2006-2015 BIO Industry Analysis).
This field is new for Turkey and civil organizations have been established and various papers have been published. Clinical Resarch Society has added “Biological Products and Biosimilars Training Program” to KADUZEM platrom (www.kaduzem.org) in 2017. Better understanding of the subject, and the positive outcome of biosimilar development and production might help Turkey to become an important player.

## Biotechnological Drugs and Clinical Trials

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The adventure of biotechnological drugs obtained from living organisms via genetic alteration, started for the first time in the beginning of 1980s with the use of human insülin, produced by recombinant DNA technology in the treatment of diabetes mellitus however the activities in the research, development and production of biotechnological drugs have increased worldwide since then. The use of biotechnological methods are more common than the conventional methods for the development of drugs used in the treatment of diseases and as a result, the number of biosimilars have started to increase rapidly. When we take a look at both the political documents and the increase in the industrial investments, obviously the importance of the research and development of biotechnological products have increased. In accordance with that, the number of clinical trials using biotechnological products, the number of volunteers and the budgets for those trials have also increased. The most common group of drugs used in those studies are monoclonal antibodies and the most common applicatons for the trials are from the oncology field. Most of the clinical trials are generally phase III, however trials for Phase II and phase I are present. The legislation for clinical research is in accordance with the international regulations. When investigating the applications for the clinical trials, in addition to our national legislation, the spesific brochures for the investigational products are also used and when necessary a view of the scientific advisory committee is also obtained. The permissions for the trials are given as a result of the mentioned evaluations. In the clinical trials performed by biotechnological drugs, the insurance is asked to cover the five year period starting from the end of the trial. The increase in the research and development of the biotechnological products worldwide and across Turkey, will significantly contribute to the increase in the knowledge(know-how), infrastructure, qualified personnel and the ability of the patients to reach the therapeutic approaches developed by the use of new biotechnological methods earlier than planned.

## Construction of Biotechnological Drug Research and Its Future

Başak Eryılmaz
AİFD Genel Sekreter Yardımcısı

Investors from the Association of Pharmaceutical Companies (AİFD) only invested in domestic production in the last 15 years a total amount of 2.5 billion dollars. AİFD members are directly involved with 8 factories in the domestic production. Multinational pharmaceutical companies currently provide employment opportunities for 10,000 people. 6 AIFD members of the regional center of our country deploying in Turkey is contributing to regional leadership role. AIFD members contribute 1 billion USD to their gross domestic product (GDP) through the employment they create. The pharmaceutical industry today is the industry that distinguishes the largest share in research and development from its sales. Total drug R & D expenditure is expected to reach 181 billion dollars by 2022. The development of a new drug, on average, is $ 2.6 billion, including the cost of failures, while the duration is over 10 years, while the development period of biosimilars is between 5-9 years on average and the cost is $ 135 million, excluding the cost of failures. The development period for complex generics is 5-7 years on average and 10-20 million dollars on drug development cost. The average time for small-molecule generic development is 2-4 years and the cost is 1-4 million dollars. When we look at the role of clinical trials in the pharmaceutical R & D chain, basic research and preclinical research constitute 23% of the budget, while clinical studies constitute 65%, approval and licensing phase constitute 3.5% and phase IV constitutes 10%. The aim of AIFD in the tenth development plan on the global clinical trials is an increase by 25% annually in Turkey on the basis of the number of years of clinical research. AİFD will serve the vision of "increasing the competitiveness of the pharmaceutical industry in the global market and bringing our country to a higher position in the world pharmaceutical value chain.

## Clinical Research in Turkey from the Eyes of SAK-DER

Berk Özdemir
Sözleşmeli Araştırma Kuruluşları Derneği (SAK-DER)

According to the Good Clinical Practices (GCP) Manual, the Contracted Research Organization (CRO-SAK) is defined as an independent organization that works in accordance with the principles of good clinical practice, in which the sponsor transfers all or part of its duties and powers related to the clinical trial with a written contract. Again, according to the GCP guideline, the sponsor may delegate all or part of its tasks related to the research to the contracted research organization; the selection of the contracted research organization is the responsibility of the sponsor; however, the final responsibility for the quality and accuracy of the research data always lies with the sponsor. Approximately 40-50% of all research budgets in the world are spent on drug R & D through CROs. According to the data registered a total of www.clinicaltrials.com as of today (completed or ongoing), 273 thousand is due to take place in the research, about 2985 of them are of them from Turkey. After being revised in this direction in the manual recording system that records the number in Turkey and from Turkey increased visibility. 80% of survey registered in the system from Turkey interventional, observational studies and the remaining 20%. Interventional studies include behavioral, drug, biological product, device, radiation, dietary supplement and procedure studies. 38% of ongoing research in the field of oncology is registered in Turkey. Clinical trials are approved by the ethics committees. standardization of processes in clinical research ethics committees in Turkey, the length of the agency agreement process, researchers payments, such as the lack of stability and ancillary staff of the research team are certain problems. The expansion of scientific university collaborations in Europe, Turkey is making lobbying to be preferred in research, university real-life data to be working with alliances, joint work with the production that the pharmaceutical industry in Turkey, medical device companies, with our recommendations for collaboration solution.

## Biotechnological Drugs and the Society of National Drug Awareness and Rational Drug Use

İsmail Balık
President of the National Drug Awareness and Rational Drug Association

Biotechnological drugs are the fastest growing group in the pharmaceutical budget. The irrational use of biologics increases the risk of side effects, increases direct and indirect costs, and imposes on the sustainability of the drug budget. To disseminate the use of rational biological / biosimilarity, physicians and patients should be educated, regulations to be made by the health authority (Health Implementation Communiqué - SUT regulations should be made, rational reimbursement and domestic biosimilar production should be accelerated and external dependence should be reduced. In 2015, the Symposium on Current Issues Symposium and SUT workshop, Rare Diseases and Orphan Drug Symposium and Orphan Drug Regulation Workshop were conducted. In 2016, our Association organized a Rational Approach to Current Issues in Pharmaceuticals and Rational Approach to Immunooncology. On the other hand, Rational Prescribing Training Meetings were organized. We have a large number of printed publications on the spread of Rational Drug Use. Approximately 60% of patients are taking medication without asking the doctor. The majority of biotechnological drugs are oncological drugs and drugs that are used in the treatment of autoimmune diseases. Globally, biosimilar drugs provide huge saving opportunities for countries' health systems. Global measures should be taken to change the biosimilar drugs under the supervision of health personnel. Such studies have shown that there is no difference in safety, efficacy and immunogenicity.

## The Common/Superior Sense which is Necessary for the Production of Biotechnological Products and Biosimilars in Turkey

Ersin Yarış
President of the Turkish Pharmacological Society

When you take a look at the trends in the production and usage dynamics the view is very clear. In the near future, most of the drugs used by the patients, will be biotechnological drugs and the number of "conventional" drugs will seriously decrease. This situation will have the therapeutic advantage. However, for the countries that can not produce but only consume, the therapeutic costs will increase and may be will exceed the limits of the social security institutions. The term biotechnological drugs was an utopia that has been co-memorated several times for a person like me who has completed his post-graduate pharmacology training in mid 90s. I do not know whether the utopia has come to us or we have reached the utopia, however the word biotechnology and biotechnological products are now real. Nowadays biotechnological products are approved in our country, and preparations are done for the production of biosimilars. That means, production moulds and consumption molds are prepared. The institutions are doing great efforts to hold one end of the rope. Of course it is nice to have variability, however it is obligatory to steer this variability to resonance for the production and a common sense. A contradictory result may cause a serious delay in reaching the target. Unfortunately, this common sense is not at the desired level. Only a superior sense can realize this resonance. On behalf of Turkish Pharmacological Society and Turkish Medical Association, I am in enviroments and commissions where such discussions are held. I could not meet a superior sense which will be able to benefit from everybody and show the way to produce drugs to reach the targets. An inevitable parameter is the presence of such superior sense.