**SUPPLEMENTARY MATERIAL**

**ENGLISH ABSTRACT**

[Biosimilars: position paper of the Austrian Pharmacological Society (APHAR)]

The term "biological" refers to a heterogeneous group of drugs produced in living organisms: hormones and cytokines, monoclonal antibodies, vaccines, heparin and related products, blood products and coagulation factors.

Vaccines exist for more than 200 years: Edward Jenner introduced the vaccine with cowpox in 1796; Emil von Behring developed serum therapy more than 100 years ago; blood products, insulin and heparin have been used for more than 60 years. These were originally obtained from human or animal material. Today, the products, in particular hormones and growth factors, are produced recombinantly—a process that was initiated only by the discovery of deoxyribonucleic acid and the feasibility to express proteins in suitable host cells.

Therefore, these genetically engineered drugs are also referred to as biologics—as compared to chemically manufactured drugs. The development of genetically engineered biologics had been groundbreaking, leading to a significant improvement in patient care because these drugs became available without limitation. They abolished the dependence on protein agents derived from animal sources, e.g., insulin. In addition, animal protein-associated allergen cases have decreased markedly due to the use of human protein sequences. Substantial evidence was provided by the rigorous testing and approval of these genetically engineered drugs: The drug group was demonstrated to be produced safely in living organisms and be purified from cell lysates or culture supernatants. This has been shown both for growth factors such as somatotropin, erythropoietin and later for granulocyte colony-stimulating factor—a prerequisite for introducing so-called biosimilars after expiry of the patents of the original products. The expansion of the possibilities of genetic engineering has led to a new regulatory requirement: these successor products of the originators have been approved as biosimilars; due to scientific considerations of the European Medicines Agency EMA (formerly EMEA), the regulatory path differs significantly from that which is required for generics.

With the exception of vaccines and heparin derivatives, all candidate biologicals are proteins. Vaccines are subject to their own approval process. The approval of orally available new anticoagulants such as dabigatran, rivaroxaban or apixaban or the subcutaneously applicable synthetic pentameric sugars such as fondaparinux, it is currently less interesting to develop biosimilar heparins. Therefore, the following consideration focuses on all other proteins that are included in the EMA guidelines for biosimilars.