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THE PH. EUR. COMMISSION CONCLUDES ITS PILOT PHASE FOR MONOGRAPHS FOR BIOTHERAPEUTICS STILL UNDER PATENT.

Since the approval of the first biological produced by recombinant DNA (rDNA) technology, recombinant human insulin, numerous biotherapeutics have received regulatory approval in Europe. European Pharmacopoeia (Ph. Eur.) monographs have been elaborated for many of these first-generation biotherapeutics (including peptide hormones, growth factors, interferons) using the multisource approach and have led to robust quality standards.

Others, such as interleukins, coagulation factors and monoclonal antibodies, have recently faced or will be facing patent expiry in the near future, which reinforces the need for public standards. This also applies to second-generation biotherapeutics, a class of modern recombinant proteins that have been engineered to alter their pharmacological activity.

The Ph. Eur. has worked with the innovators of these biotherapeutics (which are mainly single source) using an alternative monograph elaboration procedure (P4Bio pilot phase) to ensure that, when a patent for one of these products runs out, a public standard for future products is already in place. During the elaboration process, the tests and procedures described in a monograph are subjected to extensive experimental testing by European Pharmacopoeia experts from Official Medicines Control Laboratories and by the EDQM Laboratory and the draft monograph text is published for public consultation, thus ensuring the robustness of the standard. To date, four P4Bio monographs have been published in the Ph. Eur.: *Insulin glargine* (2571), *Human coagulation factor VIIa (rDNA) concentrated solution* (2534), *Human coagulation factor IX (rDNA) concentrated solution* (2522) and *Teriparatide* (2829).

The P4Bio pilot phase came to a successful conclusion at the 156th Session of the European Pharmacopoeia Commission held in Strasbourg on 22-23 November 2016, with the adoption of the monograph for *Etanercept* (2895).

The *Etanercept* monograph is further proof that the standardisation challenges related to the complexity and heterogeneity of biotherapeutics can be overcome, so that the monograph specifications are compatible with the development of biosimilars. For example, including process-dependent microheterogeneity (*e.g.* glycosylation) tests in the Production section adds flexibility to the monograph.

The P4Bio pilot phase is a success story and another positive example of the advantages of close collaboration across the scientific community, bringing together Ph. Eur. experts, European regulators and manufacturers. It clearly demonstrated that robust public standards for complex molecules, compatible with Innovation and the development of future biotherapeutic products, can be established.

[1]There are thirty-eight members of the European Pharmacopoeia Commission: *Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, the Former Yugoslav Republic of Macedonia, Turkey, Ukraine, United Kingdom and the European Union.*

The Ph. Eur. Commission has therefore decided to transform the P4Bio-Pilot Working Party into a Group of Experts.

The lessons learned during the P4Bio pilot phase have recently been published in a scientific paper (Buda M, Wicks S, Charton E. Elaborating Ph. Eur. monographs for biotherapeutic proteins using substances from a single source. *Pharmeur Bio Sci Notes* 2016: 129-134).

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Note for the Editor: Further information is available on the internet site **www.edqm.eu**
The EDQM is a leading organisation that protects public health by enabling development, supporting implementation, and monitoring the application of quality standards for safe medicines and their safe use. Our standards are recognised as a scientific benchmark world-wide. The European Pharmacopeia is legally-binding in Member States[1]. Similarly, the EDQM develops guidance and standards in the areas of blood transfusion, organ transplantation and consumer health issues.

A political organisation set up in 1949, the Council of Europe works to promote democracy and human rights continent-wide. It also develops common responses to social, cultural and legal challenges in its 47 member states.

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