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A New Era for Novel Therapies in Animal Health

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On January 28, 2022, the Veterinary Medicines Regulation (EU) 2019/6 (the EU Regulation) came into application, repealing and replacing Directive 2001/82/EC. This new modern legal framework aims — next to laying down a wide range of concrete measures to fight antimicrobial resistance (AMR) — to promote and increase the timely availability of veterinary medicinal products (VMPs) by stimulating innovation and competition. Clear rules for innovative VMP, so called "novel therapies" (e.g., gene therapies), will encourage their development. It is hoped that Switzerland, as a center of innovation, will also soon create the urgently needed legal basis to meet the demand for innovative (e.g., stem cell) therapies for animals, and that the UK will continue to modernise its regulatory framework for veterinary medicines.

Novel veterinary therapies have the potential to become an important part of future treatment strategies for animals. Research and development in this area have gathered speed significantly over the last few years, and the number of available novel therapies should continue to grow. The new EU Regulation will provide the regulatory framework and guidance for this group of complex novel therapies. In this article, we (i) examine the definition of novel therapies; (ii) explore their history; (iii) take a closer look at the new regulatory framework in the EU and according developments in Switzerland and the UK; and (iv) give an outlook on the future.

What is meant by novel therapy veterinary medicinal product?

The novel therapy category will apply to VMPs for:

- gene therapy;
- regenerative medicine and tissue engineering and cell therapy;
- blood product therapy;
- phage therapy;
- nanotechnologies;
- RNA antisense therapy and RNA interference therapy products; and
- other therapies considered as a nascent field in veterinary medicine.

History of novel therapies

Although the legal definition of "novel therapy" is new, the research and development into novel veterinary medicines has been ongoing for many years and is increasingly bearing

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fruit. This has resulted in the development of breakthrough technologies and the authorization of novel products — sometimes in advance of human medicine.

The first DNA vaccines were approved in animals, including the EU authorization for a salmon pancreas disease vaccine (recombinant DNA plasmid) in 2016. Interestingly, the years of research into DNA and mRNA vaccines enabled this technology to be quickly leveraged in response to the COVID-19 pandemic, leading to the creation of the first human DNA and mRNA vaccines.

Other landmarks in the development of novel veterinary therapies include these:

- 2017: the first EU authorization of a monoclonal antibody VMP for the treatment of dogs with atopic dermatitis
- 2019: the first EU stem cell-based VMP authorized for the treatment of lameness in horses
- 2020: the authorization in the EU of a monoclonal antibody targeting nerve growth factor (NGF) for the alleviation of pain in osteoarthritis in dogs
- 2021: the authorization in the EU of a felinized monoclonal targeting NGF for the alleviation of pain in osteoarthritis in cats

The development of these medicines, which often did not neatly fit into the categories of VMP under the existing legal framework dating from 2001, has required regulatory flexibility. The new EU Regulation looks to build on the existing knowledge and experience gained under the old regulatory framework to cater to the scientific advancements of the future.

New regulatory framework in the EU and according developments in Switzerland and the UK

The novel therapy category is an umbrella term that operates above the level of the three existing product categories. Depending on the active substance and the mode of action, a novel therapy VMP could fall under one of the three product categories:

- VMP other than biological VMP;
- biological VMP other than immunological VMP; or
- immunological VMP.

The technical documentation necessary for demonstrating the quality, safety and efficacy of all VMPs is set out in Annex II of the Regulation (as amended by Regulation 2021/805), which introduces additional requirements for novel therapies. These requirements are non-exhaustive and may be adapted on a case-by-case basis based on a risk analysis. The EU Regulation states that deviations from the requirements of Annex II are possible when

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justified — granting scope for flexibility. The operational expert groups of the Novel Therapies & Technologies Working Party plan to release further specific guidelines for consultation on efficacy of cell therapies and on quality, safety and efficacy of bacteriophages in 2022.

In addition to the premarketing requirements, the EMA anticipates that a more extensive use of post-marketing measures, including risk management plans and requests for additional post-marketing studies, should be foreseen for novel therapies.

Switzerland has, with regard to the new EU Regulation, recognized the urgent need for action and therefore intends — in particular to avoid trade barriers — to address the most important differences through selective adjustments of the national regulatory basis within an early revision of the relevant ordinances. The legislative adjustments came into force at the same time as the application of the EU Regulation. However, the creation of the currently missing legal basis to make, for example, stem cell products available to Swiss veterinary medicine has not yet been realized. The legal basis to be able to submit a corresponding application for marketing authorization approval in Switzerland (to Swissmedic) is still missing. The Swiss Transplantation Act (Federal Act of October 8, 2004, on the Transplantation of Organs, Tissues and Cells, SR 810.21), which is relevant in this case, applies only to products used on humans. There is no regulation for transplant products for use on animals. It is therefore to be hoped that the necessary foundations will be laid in the next revision of the law so that Swiss veterinarians will also be able to offer these novel therapies.

In the UK, the new EU Regulation has also not been implemented into national law, and so the UK has also confirmed temporary mitigations to bridge some of the regulatory gaps while consultations are ongoing to update the UK framework. Unlike the Swiss framework, however, veterinary stem cell therapies are already a possibility under national law. Additionally, the UK regulator has already set out its intention to develop a fit-for-purpose framework for emerging novel therapies in its 2021–2026 Regulatory Science Strategy.

What does the future hold?

The growth in novel therapies appears set to continue, enabled by new research and technology and driven by unmet need and global challenges, such as AMR (where, for example, novel bacteriophages could play an important role).

There is also great potential for novel veterinary therapies to be adapted and developed for humans (such as advanced therapy medicinal products) and vice versa. Indeed, as animals are often used as models for human disease, this preclinical data can be a valuable resource for the development of treatments for animals themselves.

It is hoped that the promotion of innovation and development of novel therapies will be further facilitated through the (i) overdue creation of hitherto missing legal foundations in Switzerland, (ii) the proposed adaptation of regulatory framework in the UK and (iii) the implementation of the new EU Regulation in the EU. The appropriate balance of guidance

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and flexibility should encourage innovative companies to develop novel therapies and enable a new era of novel therapy veterinary medicine product development.

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